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* * * * * * * * * * Welcome to STN International * * * * * * * * * *

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 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  JAN 02  STN pricing information for 2008 now available
 NEWS  3  JAN 16  CAS patent coverage enhanced to include exemplified
                  prophetic substances
 NEWS  4  JAN 28  USPATFULL, USPAT2, and USPATOLD enhanced with new
                  custom IPC display formats
 NEWS  5  JAN 28  MARPAT searching enhanced
 NEWS  6  JAN 28  USGENE now provides USPTO sequence data within 3 days
                  of publication
 NEWS  7  JAN 28  TOXCENTER enhanced with reloaded MEDLINE segment
 NEWS  8  JAN 28  MEDLINE and LMEDLINE reloaded with enhancements
 NEWS  9  FEB 08  STN Express, Version 8.3, now available
 NEWS 10  FEB 20  PCI now available as a replacement to DPCI
 NEWS 11  FEB 25  IFIREF reloaded with enhancements
 NEWS 12  FEB 25  IMSPRODUCT reloaded with enhancements
 NEWS 13  FEB 29  WPINDEX/WPIDS/WPIX enhanced with ECLA and current
                  U.S. National Patent Classification
 NEWS 14  MAR 31  IFICDB, IFIPAT, and IFIUDB enhanced with new custom
                  IPC display formats
 NEWS 15  MAR 31  CAS REGISTRY enhanced with additional experimental
                  spectra
 NEWS 16  MAR 31  CA/CAplus and CASREACT patent number format for U.S.
                  applications updated
 NEWS 17  MAR 31  LPCI now available as a replacement to LDPCI
 NEWS 18  MAR 31  EMBASE, EMBAL, and LEMBASE reloaded with enhancements
 NEWS 19  APR 04  STN AnaVist, Version 1, to be discontinued
 NEWS 20  APR 15  WPIDS, WPINDEX, and WPIX enhanced with new
                  predefined hit display formats
 NEWS 21  APR 28  EMBASE Controlled Term thesaurus enhanced
 NEWS 22  APR 28  IMSRESEARCH reloaded with enhancements

 NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8
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Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:24:16 ON 19 MAY 2008

=> file reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 12:24:24 ON 19 MAY 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 18 MAY 2008 HIGHEST RN 1021422-05-8
DICTIONARY FILE UPDATES: 18 MAY 2008 HIGHEST RN 1021422-05-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

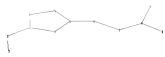
TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10763974\Struc 6.str



chain nodes :
6 7 8 9 10 11 12
ring nodes :
1 2 3 4 5
chain bonds :
1-6 3-11 6-7 7-8 8-9 8-10 11-12
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 1-6 2-3 3-4 3-11 4-5 6-7 7-8 8-9 8-10 11-12

G1:C,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:Atom 10:Atom
11:CLASS 12:Atom

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L1      STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1              STR
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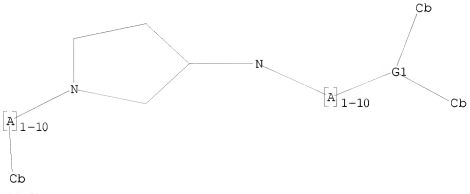


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Structure attributes must be viewed using STN Express query preparation.


=> l1
SAMPLE SEARCH INITIATED 12:24:38 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    14571 TO ITERATE

 13.7% PROCESSED     2000 ITERATIONS                                0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:       284189 TO   298651
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> l1 full
FULL SEARCH INITIATED 12:24:53 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   289101 TO ITERATE

100.0% PROCESSED   289101 ITERATIONS                              90 ANSWERS
SEARCH TIME: 00.00.05

L3           90 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             178.36     178.57

FILE 'CAPLUS' ENTERED AT 12:25:06 ON 19 MAY 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 19 May 2008 VOL 148 ISS 21
FILE LAST UPDATED: 18 May 2008 (20080518/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/legal/infopolicy.html

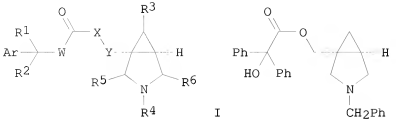
=> l3
L4 24 L3

=> d ibib abs hitstr 1-24

L4 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1375122 CAPLUS
DOCUMENT NUMBER: 148:239019
TITLE: Substituted azabicyclohexane derivatives as muscarinic receptor antagonists and their preparation, pharmaceutical compositions and use in the treatment of respiratory, urinary and gastrointestinal diseases
INVENTOR(S): Metha, Anita; Silamkoti, Arundutt V.; Gupta, Jang B.
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, S. Afr.
SOURCE: S. African, 46pp.
CODEN: SFXXAB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| ZA 2005008200 | A | 20060726 | ZA 2005-8200 | 20051011 |
| PRIORITY APPLN. INFO.: | | | ZA 2005-8200 | 20051011 |

OTHER SOURCE(S): CASREACT 148:239019
GI



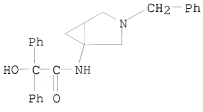
I II

AB The invention relates to derivs. of substituted azabicyclo[3.1.0]hexanes of formula I. The compds. of formula I can function as muscarinic receptor antagonists, and can be used in the treatment of various diseases of respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors. The invention also relates to the preparation of compds. of formula I, pharmaceutical compns. containing them and methods for treating diseases mediated through muscarinic receptors. Compds. of formula I wherein Ar is (un)substituted (hetero)aryl; R1 is H, OH, CH2OH, amino, alkoxy, carbamoyl and halo; R2 is H, alkyl, C3-7 cycloalkyl, C3-7 cycloalkenyl and (un)substituted (hetero)aryl; W is (CH2)0-1; X is O, S, NH and derivs., and absent; Y is (CH2)0-1; R3, R5 and R6 are independently H, lower alkyl, CO2H, CONH2, NH2 and CH2NH2; R4 is H, C1-15 (un)substituted (un)saturated (un)branched aliphatic hydrocarbon; and their pharmaceutically acceptable salts, pharmaceutically acceptable solvates, esters, enantiomers, diastereoisomers, N-oxides, polymorphs, and metabolites thereof, are claimed. Example compound II was prepared by esterification of 3-benzyl-3-azabicyclo[3.1.0]hexane-1-carboxylic acid; the resulting 3-benzyl-3-azabicyclo[3.1.0]hexane-1-carboxylic acid Et ester underwent hydride reduction to give 3-benzyl-1-hydroxymethyl-3-azabicyclo[3.1.0]hexane, which underwent sulfonylation and amidation with diphenylglycolic acid to give compound II. All the invention compds. were evaluated for their muscarinic antagonistic activity. From the assay, it was determined that compound II exhibited pKi values of 7.71 and 7.95 against M2
and M3 resp.

IT 777890-69-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted azabicyclohexane derivs. as muscarinic receptor antagonists useful in the treatment of respiratory, urinary and gastrointestinal diseases)

RN 777890-69-4 CAPLUS

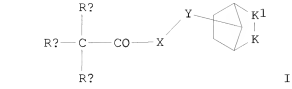
CN Benzeneacetamide, α-hydroxy-α-phenyl-N-[3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-1-yl]- (CA INDEX NAME)



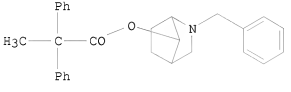
L4 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1114104 CAPLUS
DOCUMENT NUMBER: 147:427240
TITLE: Preparation of azabicyclo[2.2.1]heptyl compounds as muscarinic receptor antagonists for treating respiratory, urinary, and gastrointestinal disorders
INVENTOR(S): Kumar, Naresh; Cliffe, Ian Anthony; Salman, Mohammad; Palle, Venkata P.; Kaur, Kirandeep; Shejul, Yogesh D.; Chugh, Anita; Gupta, Suman; Ray, Abhijit; Malhotra, Shivani; Shirumalla, Raj Kumar
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007110782 | A1 | 20071004 | WO 2007-IB50003 | 20070102 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |

PRIORITY APPLN. INFO.: IN 2005-DE3522 A 20051230
OTHER SOURCE(S): CASREACT 147:427240; MARPAT 147:427240
GI




I



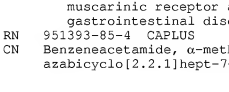

II

AB This present invention generally relates to muscarinic receptor antagonists of general formula I (wherein K is -CH2 and K1 is -NR1 or K1 is -CH2 and K is -NR1 (wherein R1 is H, alkyl, aryl, etc.); Y is alkylene or a single bond; X is O, S or -NR5 (wherein R5 is H, alkyl, etc.); Ra is OH, alkoxy, alkyl or H; Rb and Rc are alkyl, alkenyl, alkynyl, etc.) which are useful, among other uses, for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors. The invention also relates to the process for the preparation of disclosed compds., pharmaceutical compns. containing the disclosed compds., and the methods for treating diseases mediated through muscarinic receptors. Example compound II was prepared by reacting 2,2-diphenylpropanoic acid and 2-benzyl-7-bromo-2-azabicyclo[2.2.1]heptane. In radioligand binding assays, II had Ki values for rat M2 and M3 receptors in the range 2 - >500 nM.

IT 951393-85-4P, N-(2-Benzyl-2-azabicyclo[2.2.1]hept-7-yl)-2,2-diphenylpropanamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of azabicyclo[2.2.1]heptyl compds. as muscarinic receptor antagonists for treating respiratory, urinary, and gastrointestinal disorders)

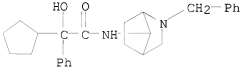
RN 951393-85-4 CAPLUS

CN Benzeneacetamide, α-methyl-α-phenyl-N-[2-(phenylmethyl)-2-azabicyclo[2.2.1]hept-7-yl]- (CA INDEX NAME)

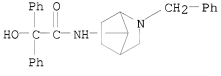



IT 951393-96-7P, N-(2-Benzyl-2-azabicyclo[2.2.1]hept-7-yl)-2-cyclopentyl-2-hydroxy-2-phenylacetamide 951393-98-9P,

N-(2-Benzyl-2-azabicyclo[2.2.1]hept-7-yl)-2-hydroxy-2,2-diphenylacetamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of azabicyclo[2.2.1]heptyl compds. as muscarinic receptor antagonists for treating respiratory, urinary, and gastrointestinal disorders)
RN 951393-96-7 CAPLUS
CN Benzeneacetamide, α-cyclopentyl-α-hydroxy-N-[2-(phenylmethyl)-2-azabicyclo[2.2.1]hept-7-yl]- (CA INDEX NAME)



RN 951393-98-9 CAPLUS
CN Benzeneacetamide, α-hydroxy-α-phenyl-N-[2-(phenylmethyl)-2-azabicyclo[2.2.1]hept-7-yl]- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:726515 CAPLUS
DOCUMENT NUMBER: 147:143271
TITLE: Preparation of pyrrolidine derivatives as Cannabinoid receptor (CB1) antagonists
INVENTOR(S): Moritani, Yasunori; Kokubo, Shigeru; Tsuboi, Yasunori; Okagaki, Chieko; Oku, Akira; Hirano, Naomitsu
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 222pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 2007169270 | A | 20070705 | JP 2006-316427 | 20061124 |
| PRIORITY APPLN. INFO.: | | | JP 2005-339547 A | 20051125 |

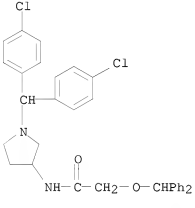
OTHER SOURCE(S): MARPAT 147:143271
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

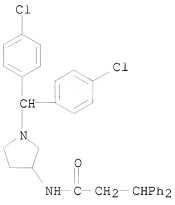
AB Title compds. [I; R1 and R2 independently = (un)substituted aryl, heteroaryl or together they may form benzocycloheptane; R3 and R4 independently = H, OH, hydroxyalkyl, etc. or together they may form an oxo group; R5 = H or alkyl; Y = single bond, O or -NR7-; R6 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R7 = alkyl or alkyloxycarbonylalkyl with provisions] and their pharmaceutically acceptable salts, are prepared and disclosed as antagonists of CB1 receptor. Thus, e.g., compound (II) was prepared by benzoylation of (3R)-1-[bis-(4-chlorophenyl)methyl]-3-aminopyrrolidine (preparation given) with 4-(trifluoromethoxy)benzoyl chloride. I as antagonists of CB1 receptor should prove useful in the treatment of diseases such as but not limited to depression, migraine and obesity. Pharmaceutical compns. comprising I are disclosed.

IT 870626-02-1P 870626-37-2P 870626-40-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidine derivs. as Cannabinoid receptor (CB1) antagonists)

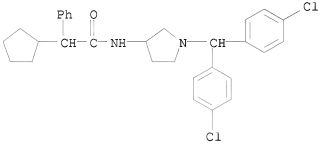
RN 870626-02-1 CAPLUS
CN Acetamide, N-[1-[bis(4-chlorophenyl)methyl]-3-pyrrolidinyl]-2-(diphenylmethoxy)- (CA INDEX NAME)




RN 870626-37-2 CAPLUS
CN Benzenepropanamide, N-[1-[bis(4-chlorophenyl)methyl]-3-pyrrolidinyl]-β-phenyl- (CA INDEX NAME)



RN 870626-40-7 CAPLUS
CN Benzeneacetamide, N-[1-[bis(4-chlorophenyl)methyl]-3-pyrrolidinyl]-α-cyclopentyl- (CA INDEX NAME)

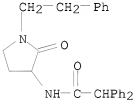


L4 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:531684 CAPLUS
DOCUMENT NUMBER: 147:166597
TITLE: Solid-phase synthesis of multiple classes of peptidomimetics from versatile resin-bound aldehyde intermediates
AUTHOR(S): Scott, William L.; Martynow, Jacek G.; Huffman, John C.; O'Donnell, Martin J.
CORPORATE SOURCE: Department of Chemistry and Chemical Biology, Indiana University Purdue University Indianapolis, Indianapolis, IN, 46202-3274, USA
SOURCE: Journal of the American Chemical Society (2007), 129(22), 7077-7088
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 147:166597
AB A wide variety of highly substituted lactam containing peptidomimetic scaffolds were prepared by solid-phase synthesis from a single, versatile class of resin-bound aldehyde intermediates. These included monocyclics, bicyclics, tricyclics, and tetracyclics. The key intermediate was readily

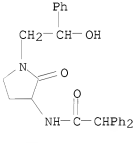
synthesized from resin-bound natural or unnatural α-amino acids. The synthetic procedures permitted the construction of a large diversity of substitution patterns for ready use in combinatorial chemical In every case, the release of final products from resin was achieved by a cyclitive cleavage process. Since this depends on successful completion of multiple intermediate synthetic steps, the products are often quite pure, even though previous steps involve only a filtration workup. The mild conditions for many of these synthetic procedures offered the promise of using this chemical in peptide fragment condensations to produce modified peptides, at either the N-terminus or C-terminus, or as individually assembled peptide segments with a wide variety of conformationally restricted peptidomimetic linkers at the point of juncture.

IT 944070-98-8P 944070-99-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase preparation of peptidomimetics using resin-boundallylamino acids and amino aldehydes as key intermediates and reductive lactonization/cleavage, reductive amination/lactamization cleavage as key steps)

RN 944070-98-8 CAPLUS
CN Benzeneacetamide, N-[2-oxo-1-(2-phenylethyl)-3-pyrrolidinyl]-α-phenyl- (CA INDEX NAME)



RN 944070-99-9 CAPLUS
CN Benzeneacetamide, N-[1-(2-hydroxy-2-phenylethyl)-2-oxo-3-pyrrolidinyl]-α-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 306 THERE ARE 306 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:295302 CAPLUS
DOCUMENT NUMBER: 144:350723
TITLE: Preparation of phenyl-substituted amine diols and related compounds as muscarinic receptor antagonists

for treating diseases such as those of the respiratory, urinary and gastrointestinal systems

INVENTOR(S): Salman, Mohammad; Sarma, Pakala Kumara Savithru; Dharmarajan, Sankaranarayanan; Chugh, Anita; Gupta, Suman

PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India

SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006032994 | A2 | 20060330 | WO 2005-IB2823 | 20050923 |
| WO 2006032994 | A3 | 20060504 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| EP 1794161 | A2 | 20070613 | EP 2005-789768 | 20050923 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| IN 2007DN01979 | A | 20070817 | IN 2007-DN1979 | 20070314 |
| PRIORITY APPLN. INFO.: | | | US 2004-613001P P | 20040924 |
| | | | WO 2005-IB2823 W | 20050923 |

OTHER SOURCE(S): CASREACT 144:350723; MARPAT 144:350723

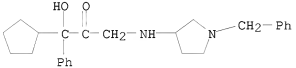
AB This present invention generally relates to muscarinic receptor antagonists (PhC(X)(OH)C(:G)CH2N(R1)(R2) (I) or PhC(X)(OH)C(G)CH2N(R1)(R2) (II); variables defined below; e.g. 1-cyclopentyl-3-([1,4]diazepan-1-yl)-1-hydroxy-1-phenylpropan-2-one), which are useful, among other uses, for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors. The invention also relates to the process for the preparation of disclosed compds., pharmaceutical compns. containing the disclosed compds., and the methods for treating diseases mediated through muscarinic receptors. For I and II: X = alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, heterocyclylalkyl, or heteroarylalkyl; R1 = H, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy, aryloxy, -(CH2)0-2-heterocyclylalkyl, or -(CH2)0-2-heteroarylalkyl; R2 = -(CH2)0-2-heteroaryl, -(CH2)0-2-heterocyclyl, or -(CH2)0-2-aryl, or R1 and R2 may together combine to form a (un)saturated monocyclic or bicyclic ring system containing 0-4 heteroatoms (O, N or S) wherein the ring can be (un)substituted with ≥1 of alkyl, alkenyl, alkynyl, cycloalkyl, alkaryl, alkoxy, aryloxy, et al.; G = -OR [R = H or unsubstituted lower (C1-C6) alkyl], -NOR, -NHYR' (R' is H, alkyl or aryl and Y is -C(O), -SO or -SO2), or O (provided that R1 and R2 together does not form a pyrrolidine, 4-hydroxypiperidine, 4-

pyrrolidinylpiperidine, piperazine or azabicyclo[3.1.0]hexane ring). Methods of preparation are claimed and prepns. and/or characterization data for .apprx.80 examples of I are included. For example, 1-cyclopentyl-1-hydroxy-1-phenyl-3-(piperidin-1-yl)propan-2-one was prepared (86 %) from piperidine, Et3N and 3-bromo-1-cyclopentyl-1-hydroxy-1-phenyl-2-propanone (preparation described) in CH2Cl2. Ki values for I tested in a radioligand binding assay range from .apprx.5 nM to .apprx.10 μM for M2 receptors, and from .apprx.0.5 nM to .apprx.10 μM for M3 receptors. Selectivity for bladder pressure inhibition vs. salivation was determined for compound 3 examples of I and was .apprx.2, similar to that determined for tolterodine.

IT 881098-12-0P, 3-[(1-Benzylpyrrolidin-3-yl)amino]-1-cyclopentyl-1-hydroxy-1-phenylpropan-2-one
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of Ph-substituted amine diols and related compds. as muscarinic receptor antagonists for treating diseases such as those of respiratory, urinary and gastrointestinal systems)

RN 881098-12-0 CAPLUS

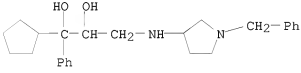
CN 2-Propanone, 1-cyclopentyl-1-hydroxy-1-phenyl-3-[[1-(phenylmethyl)-3-pyrrolidinyl]amino]- (CA INDEX NAME)



IT 881098-43-7P, 3-[(1-Benzylpyrrolidin-3-yl)amino]-1-cyclopentyl-1-phenylpropane-1,2-diol 881098-50-6P, 3-[(1-Benzylpyrrolidin-3-yl)amino]-1,1-diphenylpropane-1,2-diol 881098-74-4P, 3-[(1-Benzylpyrrolidin-3-yl)(methyl)amino]-1-cyclopentyl-1-hydroxy-1-phenylpropan-2-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of Ph-substituted amine diols and related compds. as muscarinic receptor antagonists for treating diseases such as those of respiratory, urinary and gastrointestinal systems)

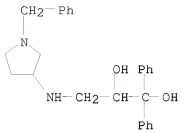
RN 881098-43-7 CAPLUS

CN 1,2-Propanediol, 1-cyclopentyl-1-phenyl-3-[[1-(phenylmethyl)-3-pyrrolidinyl]amino]- (CA INDEX NAME)

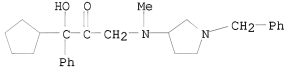


RN 881098-50-6 CAPLUS

CN 1,2-Propanediol, 1,1-diphenyl-3-[[1-(phenylmethyl)-3-pyrrolidinyl]amino]- (CA INDEX NAME)



RN 881098-74-4 CAPLUS
CN 2-Propanone, 1-cyclopentyl-1-hydroxy-3-[methyl[1-(phenylmethyl)-3-pyrrolidinyl]amino]-1-phenyl- (CA INDEX NAME)



L4 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1290266 CAPLUS
DOCUMENT NUMBER: 144:22804
TITLE: Preparation of pyrrolidine derivatives as CB1 receptor antagonists
INVENTOR(S): Moritani, Yasunori; Furukubo, Shigeru; Tsuboi, Yasunori; Okagaki, Chieko; Oku, Akira; Hirano, Naomitsu
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 205 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005115977 | A1 | 20051208 | WO 2005-JP10197 | 20050527 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| JP 2006219472 | A | 20060824 | JP 2005-155309 | 20050527 |

| | | | | | |
|---|---|---|---|---|---|
| EP 1748980 | A1 | 20070207 | EP 2005-745829 | | 20050527 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU | | | | | |
| CN 1960970 | A | 20070509 | CN 2005-80017310 | | 20050527 |
| US 20070167440 | A1 | 20070719 | US 2006-579950 | | 20061109 |
| PRIORITY APPLN. INFO.: | | | JP 2004-160059 | A | 20040528 |
| | | | US 2004-575409P | P | 20040601 |
| | | | JP 2005-7833 | A | 20050114 |
| | | | US 2005-644992P | P | 20050121 |
| | | | WO 2005-JP10197 | W | 20050527 |

OTHER SOURCE(S): MARPAT 144:22804
GI

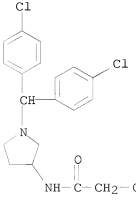
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 and R2 independently = (un)substituted aryl, heteroaryl or together they may form benzocycloheptane; R3 and R4 independently = H, OH, hydroxyalkyl, etc. or together they may form an oxo group; R5 = H or alkyl; Y = single bond, O or -NR7-; R6 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R7 = alkyl or alkyloxycarbonylalkyl with provisions] and their pharmaceutically acceptable salts, are prepared and disclosed as antagonists of CB1 receptor. Thus, e.g., II was prepared by benzoylation of (3R)-1-[bis-(4-chlorophenyl)methyl]-3-aminopyrrolidine (preparation given) with 4-(trifluoromethoxy)benzoyl chloride. I as antagonists of CB1 receptor should prove useful in the treatment of diseases such as but not limited to depression, migraine and obesity. Pharmaceutical compns. comprising I are disclosed.

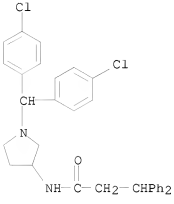
IT 870626-02-1P 870626-37-2P 870626-40-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidine derivs. as CB1 receptor antagonists)

RN 870626-02-1 CAPLUS

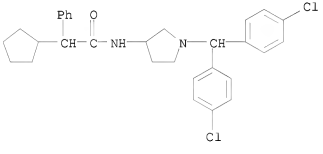
CN Acetamide, N-[1-[bis(4-chlorophenyl)methyl]-3-pyrrolidinyl]-2-(diphenylmethoxy)- (CA INDEX NAME)



RN 870626-37-2 CAPLUS
CN Benzenepropanamide, N-[1-[bis(4-chlorophenyl)methyl]-3-pyrrolidinyl]-β-phenyl- (CA INDEX NAME)



RN 870626-40-7 CAPLUS
CN Benzeneacetamide, N-[1-[bis(4-chlorophenyl)methyl]-3-pyrrolidinyl]-α-cyclopentyl- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

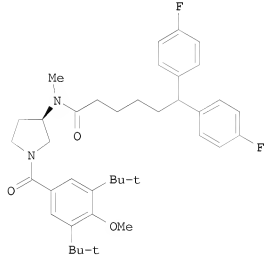
L4 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:672888 CAPLUS
DOCUMENT NUMBER: 143:172750
TITLE: Preparation of 3-aminopyrrolidine useful as N-type calcium channel blockers
INVENTOR(S): Pajouhesh, Hassan; Pajouhesh, Hossein; Ding, Yanbing; Snutch, Terrance P.
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 41 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| US 20050165065 | A1 | 20050728 | US 2004-763974 | 20040122 |
| AU 2005206226 | A1 | 20050804 | AU 2005-206226 | 20050121 |
| CA 2553773 | A1 | 20050804 | CA 2005-2553773 | 20050121 |
| WO 2005070919 | A1 | 20050804 | WO 2005-CA73 | 20050121 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1718633 | A1 | 20061108 | EP 2005-700289 | 20050121 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS | | | | |
| CN 1976920 | A | 20070606 | CN 2005-80006161 | 20050121 |
| BR 2005007054 | A | 20070612 | BR 2005-7054 | 20050121 |
| JP 2007518742 | T | 20070712 | JP 2006-549809 | 20050121 |
| IN 2006KN02111 | A | 20070518 | IN 2006-KN2111 | 20060726 |
| PRIORITY APPLN. INFO.: | | | US 2004-763974 A | 20040122 |
| | | | WO 2005-CA73 W | 20050121 |

OTHER SOURCE(S): CASREACT 143:172750; MARPAT 143:172750

GI




I

AB Title compds. I, II; X1 = N, CR3; W = L2A3, X1A1A2; L1, L2 = (substituted) alkylene, alkenylene optionally interrupted by N, O, S; A1, A2, A3 = (fused) (substituted) 6-7 membered (hetero)aliphatyl, (hetero)aryl; R1, R2 = noninterfering substituent; R3 = H, noninterfering substituent; n = 0-3; [with a proviso], were prepared The invention compds. generally contain ≥1 benzhydryl moiety, and are useful in treating conditions which benefit from blocking calcium ion channels. For instance,

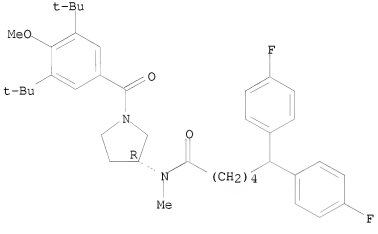
3-aminopyrrolidine derivative III (IC50 at 0.067 Hz: 67 nM) was prepared via amidation of 6,6-bis-(4-fluorophenyl)hexanoic acid by (R)-(1-benzylpyrrolidin-3-yl)(methyl)amine, N-debenzylation, and subsequent amidation of the obtained aminopyrrolidine derivative by 3,5-di-tert-butyl-4-methoxybenzoic acid.

IT 861104-36-1P 861104-39-4P 861104-41-8P
861104-42-9P 861104-46-3P 861104-47-4P
861104-48-5P 861104-50-9P 861104-51-0P
861104-52-1P 861104-56-5P 861104-58-7P
861104-59-8P 861104-60-1P 861104-61-2P
861104-62-3P 861104-63-4P 861104-64-5P
861104-66-7P 861104-68-9P 861104-70-3P
861104-72-5P 861104-76-9P 861104-77-0P
861104-78-1P 861104-79-2P 861104-80-5P
861104-81-6P 861104-82-7P 861104-92-9P
861104-95-2P 861104-98-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-aminopyrrolidine derivs. useful as N-type calcium channel blockers)

RN 861104-36-1 CAPLUS

CN Benzenehexanamide, N-[(3R)-1-[3,5-bis(1,1-dimethylethyl)-4-methoxybenzoyl]-3-pyrrolidinyl]-4-fluoro-ε-(4-fluorophenyl)-N-methyl- (CA INDEX NAME)

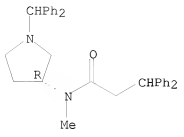
Absolute stereochemistry.




RN 861104-39-4 CAPLUS

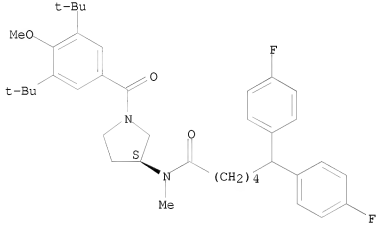
CN Benzenepropanamide, N-[(3R)-1-(diphenylmethyl)-3-pyrrolidinyl]-N-methyl-β-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



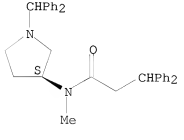
RN 861104-41-8 CAPLUS
CN Benzenehexanamide, N-[(3S)-1-[3,5-bis(1,1-dimethylethyl)-4-methoxybenzoyl]-3-pyrrolidinyl]-4-fluoro-ε-(4-fluorophenyl)-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



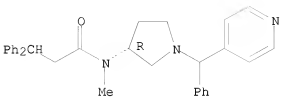
RN 861104-42-9 CAPLUS
CN Benzenepropanamide, N-[(3S)-1-(diphenylmethyl)-3-pyrrolidinyl]-N-methyl-β-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



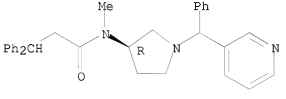
RN 861104-46-3 CAPLUS
CN Benzenepropanamide, N-methyl-β-phenyl-N-[(3R)-1-(phenyl-4-pyridinylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



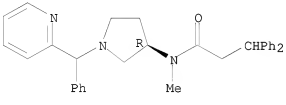
RN 861104-47-4 CAPLUS
CN Benzenepropanamide, N-methyl-β-phenyl-N-[(3R)-1-(phenyl-3-pyridinylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



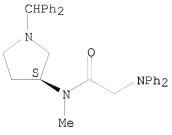
RN 861104-48-5 CAPLUS
CN Benzenepropanamide, N-methyl-β-phenyl-N-[(3R)-1-(phenyl-2-pyridinylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



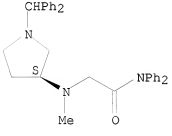
RN 861104-50-9 CAPLUS
CN Acetamide, 2-(diphenylamino)-N-[(3S)-1-(diphenylmethyl)-3-pyrrolidinyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



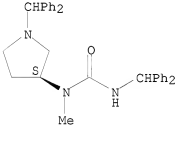
RN 861104-51-0 CAPLUS
CN Acetamide, 2-[[(3S)-1-(diphenylmethyl)-3-pyrrolidinyl]methylamino]-N,N-diphenyl- (CA INDEX NAME)

Absolute stereochemistry.



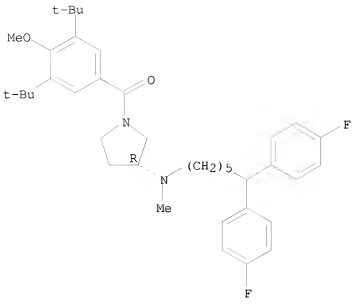
RN 861104-52-1 CAPLUS
CN Urea, N'-(diphenylmethyl)-N-[(3S)-1-(diphenylmethyl)-3-pyrrolidinyl]-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



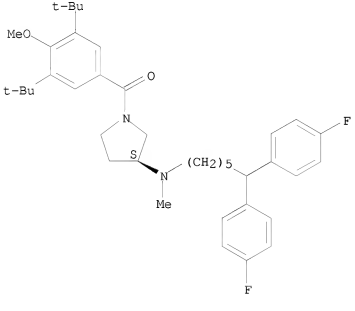
RN 861104-56-5 CAPLUS
CN Methanone, [3,5-bis(1,1-dimethylethyl)-4-methoxyphenyl][(3R)-3-[[6,6-bis(4-fluorophenyl)hexyl]methylamino]-1-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



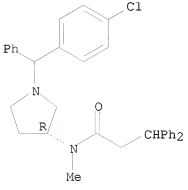

RN 861104-58-7 CAPLUS
CN Methanone, [3,5-bis(1,1-dimethylethyl)-4-methoxyphenyl][(3S)-3-[[6,6-bis(4-fluorophenyl)hexyl]methylamino]-1-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



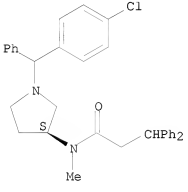

RN 861104-59-8 CAPLUS
CN Benzenepropanamide, N-[(3R)-1-[(4-chlorophenyl)phenylmethyl]-3-pyrrolidinyl]-N-methyl-β-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



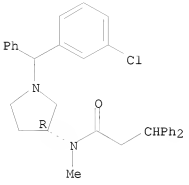

RN 861104-60-1 CAPLUS
CN Benzenepropanamide, N-[(3S)-1-[(4-chlorophenyl)phenylmethyl]-3-pyrrolidinyl]-N-methyl-β-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



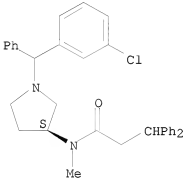

RN 861104-61-2 CAPLUS
CN Benzenepropanamide, N-[(3R)-1-[(3-chlorophenyl)phenylmethyl]-3-pyrrolidinyl]-N-methyl-β-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



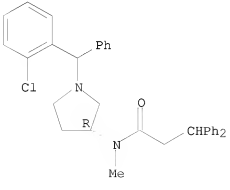

RN 861104-62-3 CAPLUS
CN Benzenepropanamide, N-[(3S)-1-[(3-chlorophenyl)phenylmethyl]-3-pyrrolidinyl]-N-methyl-β-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



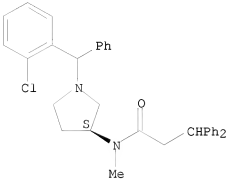

RN 861104-63-4 CAPLUS
CN Benzenepropanamide, N-[(3R)-1-[(2-chlorophenyl)phenylmethyl]-3-pyrrolidinyl]-N-methyl-β-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



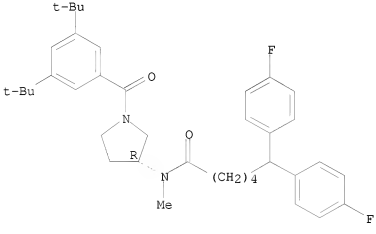
RN 861104-64-5 CAPLUS
CN Benzenepropanamide, N-[(3S)-1-[(2-chlorophenyl)phenylmethyl]-3-pyrrolidinyl]-N-methyl-β-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



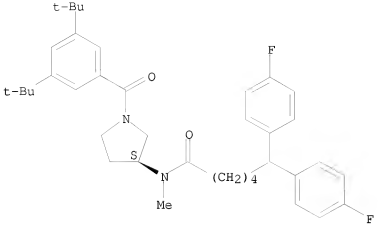

RN 861104-66-7 CAPLUS
CN Benzenehexanamide, N-[(3R)-1-[3,5-bis(1,1-dimethylethyl)benzoyl]-3-pyrrolidinyl]-4-fluoro-ε-(4-fluorophenyl)-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



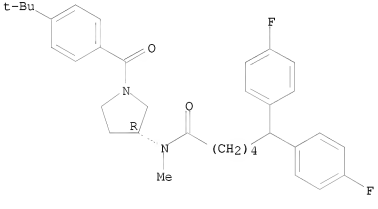

RN 861104-68-9 CAPLUS
CN Benzenehexanamide, N-[(3S)-1-[3,5-bis(1,1-dimethylethyl)benzoyl]-3-pyrrolidinyl]-4-fluoro-ε-(4-fluorophenyl)-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



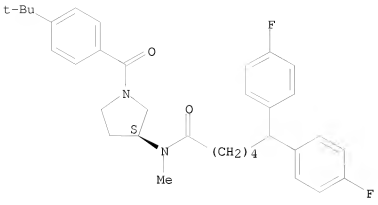

RN 861104-70-3 CAPLUS
CN Benzenehexanamide, N-[(3R)-1-[4-(1,1-dimethylethyl)benzoyl]-3-pyrrolidinyl]-4-fluoro-ε-(4-fluorophenyl)-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.



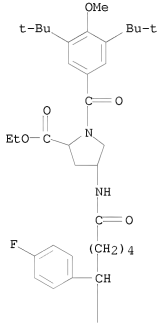

RN 861104-72-5 CAPLUS
CN Benzenehexanamide, N-[(3S)-1-[4-(1,1-dimethylethyl)benzoyl]-3-pyrrolidinyl]-4-fluoro-ε-(4-fluorophenyl)-N-methyl- (CA INDEX NAME)

Absolute stereochemistry.

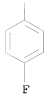



RN 861104-76-9 CAPLUS
CN Proline, 1-[3,5-bis(1,1-dimethylethyl)-4-methoxybenzoyl]-4-[[6,6-bis(4-fluorophenyl)-1-oxohexyl]amino]-, ethyl ester (CA INDEX NAME)

PAGE 1-A

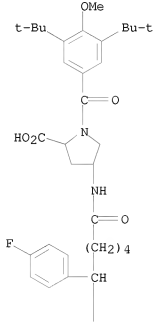


PAGE 2-A



RN 861104-77-0 CAPLUS
CN Proline, 1-[3,5-bis(1,1-dimethylethyl)-4-methoxybenzoyl]-4-[[6,6-bis(4-fluorophenyl)-1-oxohexyl]amino]- (CA INDEX NAME)

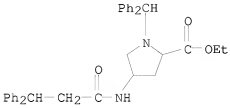
PAGE 1-A



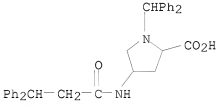
PAGE 2-A

RN 861104-78-1 CAPLUS
CN Proline, 1-(diphenylmethyl)-4-[(1-oxo-3,3-diphenylpropyl)amino]-, ethyl

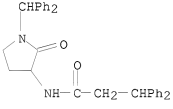
ester (CA INDEX NAME)



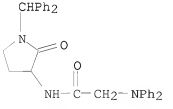
RN 861104-79-2 CAPLUS
CN Proline, 1-(diphenylmethyl)-4-[(1-oxo-3,3-diphenylpropyl)amino]- (CA INDEX NAME)



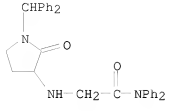
RN 861104-80-5 CAPLUS
CN Benzenepropanamide, N-[1-(diphenylmethyl)-2-oxo-3-pyrrolidinyl]-β-phenyl- (CA INDEX NAME)



RN 861104-81-6 CAPLUS
CN Acetamide, 2-(diphenylamino)-N-[1-(diphenylmethyl)-2-oxo-3-pyrrolidinyl]- (CA INDEX NAME)

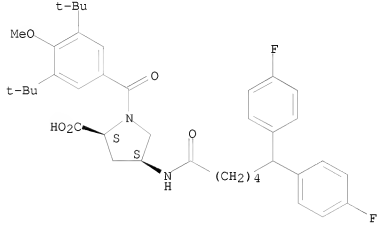


RN 861104-82-7 CAPLUS
CN Acetamide, 2-[[1-(diphenylmethyl)-2-oxo-3-pyrrolidinyl]amino]-N,N-diphenyl- (CA INDEX NAME)



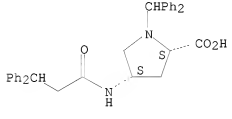
RN 861104-92-9 CAPLUS
CN L-Proline, 1-[3,5-bis(1,1-dimethylethyl)-4-methoxybenzoyl]-4-[[6,6-bis(4-fluorophenyl)-1-oxohexyl]amino]-, (4S)- (CA INDEX NAME)

Absolute stereochemistry.

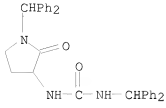


RN 861104-95-2 CAPLUS
CN L-Proline, 1-(diphenylmethyl)-4-[(1-oxo-3,3-diphenylpropyl)amino]-, (4S)- (CA INDEX NAME)

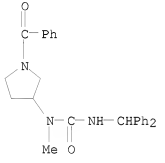
Absolute stereochemistry.



RN 861104-98-5 CAPLUS
CN Urea, N-(diphenylmethyl)-N'-[1-(diphenylmethyl)-2-oxo-3-pyrrolidinyl]- (CA INDEX NAME)

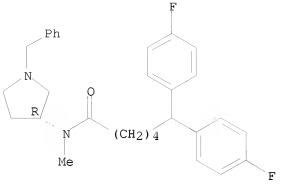


IT 861104-86-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 3-aminopyrrolidine derivs. useful as N-type calcium channel blockers)
RN 861104-86-1 CAPLUS
CN Urea, N-(1-benzoyl-3-pyrrolidinyl)-N'-(diphenylmethyl)-N-methyl- (CA INDEX NAME)



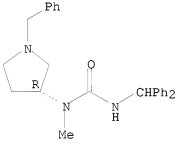
IT 861104-35-0P 861104-83-8P 861104-87-2P
861104-89-4P 861104-91-8P 861104-93-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3-aminopyrrolidine derivs. useful as N-type calcium channel blockers)
RN 861104-35-0 CAPLUS
CN Benzenehexanamide, 4-fluoro-ε-(4-fluorophenyl)-N-methyl-N-[(3R)-1-(phenylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



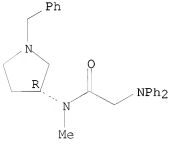
RN 861104-83-8 CAPLUS
CN Urea, N'-(diphenylmethyl)-N-methyl-N-[(3R)-1-(phenylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



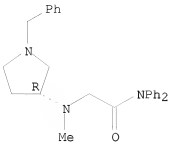
RN 861104-87-2 CAPLUS
CN Acetamide, 2-(diphenylamino)-N-methyl-N-[(3R)-1-(phenylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



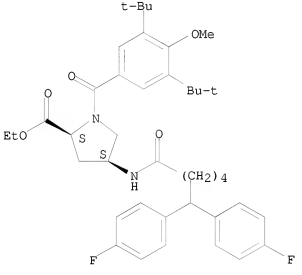
RN 861104-89-4 CAPLUS
CN Acetamide, 2-[methyl[(3R)-1-(phenylmethyl)-3-pyrrolidinyl]amino]-N,N-diphenyl- (CA INDEX NAME)

Absolute stereochemistry.



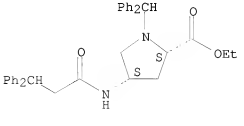

RN 861104-91-8 CAPLUS
CN L-Proline, 1-[3,5-bis(1,1-dimethylethyl)-4-methoxybenzoyl]-4-[[6,6-bis(4-fluorophenyl)-1-oxohexyl]amino]-, ethyl ester, (4S)- (CA INDEX NAME)

Absolute stereochemistry.

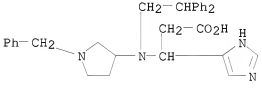



RN 861104-93-0 CAPLUS
CN L-Proline, 1-(diphenylmethyl)-4-[(1-oxo-3,3-diphenylpropyl)amino]-, ethyl ester, (4S)- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:199497 CAPLUS
DOCUMENT NUMBER: 142:430196
TITLE: Novel β-(imidazol-4-yl)-β-amino acids: solid-phase synthesis and study of their inhibitory activity against geranylgeranyl protein transferase type I
AUTHOR(S): Saha, Ashis K.; End, David W.
CORPORATE SOURCE: Janssen Research Foundation, Spring House, PA, 19477, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(6), 1713-1719
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:430196
AB Solid-phase synthesis of imidazolyl-β-amino acid derivs. is described. Several analogs demonstrated moderate inhibition of geranylgeranyl protein transferase type I (GGPT I).
IT 850883-74-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solid-phase synthesis and inhibitory activity against geranylgeranyl protein transferase type I of β-(imidazol-4-yl)-β-amino acids)
RN 850883-74-8 CAPLUS
CN 1H-Imidazole-5-propanoic acid, β-[(2,2-diphenylethyl)[1-(phenylmethyl)-3-pyrrolidinyl]amino]- (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:150038 CAPLUS
DOCUMENT NUMBER: 142:403437
TITLE: Properties and structure-activity studies of cyclic β-hairpin peptidomimetics based on the cationic antimicrobial peptide protegrin I
AUTHOR(S): Robinson, John A.; Shankaramma, Sasalu C.; Jetter, Peter; Kienzl, Ursula; Schwendener, Reto A.; Vrijbloed, Jan W.; Obrecht, Daniel
CORPORATE SOURCE: Institute of Organic Chemistry, University of Zurich, Zurich, 8057, Switz.
SOURCE: Bioorganic & Medicinal Chemistry (2005), 13(6), 2055-2064
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.

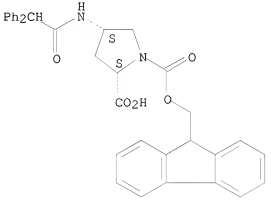
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:403437

AB The properties and structure-activity relationships (SAR) of a macrocyclic analog of porcine protegrin I (PG-I) have been investigated. The lead compound, having the sequence cyclo(Leu-Arg-Leu-Lys-Lys-Arg-Arg-Trp-Lys-Tyr-Arg-Val-D-Pro-Pro), shows antimicrobial activity against Gram-pos. and -neg. bacteria, but a much lower hemolytic activity and a much reduced ability to induce dye release from phosphatidylcholine/phosphatidylglycero l liposomes, when compared to PG-I. The enantiomeric form of the lead peptide shows comparable antimicrobial activity, a property shared with other cationic antimicrobial peptides acting on cell membranes. SAR studies involving the synthesis and biol. profiling of over 100 single site substituted analogs, showed that the antimicrobial activity was tolerant to a large number of the substitutions tested. Some analogs showed slightly improved antimicrobial activities (2-4-fold lowering of MICs), whereas other substitutions caused large increases in hemolytic activity on human red blood cells.

IT 458546-92-4P
RL: CRT (Combinatorial reactant); RCT (Reactant); SPN (Synthetic preparation); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)
(properties and structure-activity studies of cyclic β-hairpin peptidomimetics based on cationic antimicrobial peptide protegrin I)

RN 458546-92-4 CAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(diphenylacetyl)amino]-, 1-(9H-fluoren-9-ylmethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



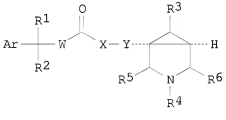
REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:878286 CAPLUS
DOCUMENT NUMBER: 141:366133
TITLE: Preparation of substituted azabicyclo hexane derivatives as muscarinic receptor antagonists
INVENTOR(S): Mehta, Anita; Silamkoti, Arundutt Viswanatham
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India; Gupta, Jang Bahadur

SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004089363 | A1 | 20041021 | WO 2003-IB1333 | 20030410 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2521788 | A1 | 20041021 | CA 2003-2521788 | 20030410 |
| AU 2003214535 | A1 | 20041101 | AU 2003-214535 | 20030410 |
| EP 1615634 | A1 | 20060118 | EP 2003-710114 | 20030410 |
| EP 1615634 | B1 | 20070516 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003018242 | A | 20060404 | BR 2003-18242 | 20030410 |
| JP 2006514978 | T | 20060518 | JP 2004-570503 | 20030410 |
| CN 1794984 | A | 20060628 | CN 2003-826537 | 20030410 |
| AT 362364 | T | 20070615 | AT 2003-710114 | 20030410 |
| IN 2005DN05100 | A | 20071207 | IN 2005-DN5100 | 20051108 |
| US 20070287732 | A1 | 20071213 | US 2007-552617 | 20070316 |

PRIORITY APPLN. INFO.: WO 2003-IB1333 W 20030410
OTHER SOURCE(S): CASREACT 141:366133; MARPAT 141:366133
GI

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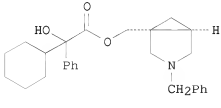



II

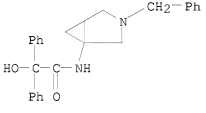
AB This invention generally relates to preparation of derivs. of substituted

azabicyclo hexanes of formula I [Ar = (un)substituted-aryl or -heteroaryl ring; R1 = H, OH, HOCH2, amino, alkoxy, carbamoyl or halo; R2 = H, alkyl, cycloalkyl, cycloalkenyl, (un)substituted-aryl or -heteroaryl ring; W = (CH2)p, where p = 0-1; X = O, S, bond, NH, or alkylamine; Y = (CH2)q, where q = 0-1; R3-5 independently = H, alkyl, CO2H, CONH2, NH2, CH2NH2; R4 = H, (un)substituted, (un)saturated-aliphatic hydrocarbon], and their pharmaceutically acceptable salts, with ability to function as muscarinic receptor antagonists. Thus, e.g., II was prepared by reaction of 2-cyclohexyl-2-hydroxy-2-phenylacetic acid with 3-benzyl-1-methanesulfonylmethyl-5-azabicyclo[3.1.0]hexane (preparation given). In receptor binding assays, I possessed pKi's ranging from 4.8-9.16 for M2- and 5.1-8.74 for M3-muscarinic receptor subtypes. I, as muscarinic receptor antagonists, can be used for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors. The invention also relates to a process for the preparation of the compds. of the present invention, pharmaceutical compns. containing the compds. of the present invention and the methods of treating the diseases mediated through muscarinic receptors.

IT 777890-69-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of azabicyclohexane derivs. as muscarinic receptor antagonists useful for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems)

RN 777890-69-4 CAPLUS

CN Benzeneacetamide, α-hydroxy-α-phenyl-N-[3-(phenylmethyl)-3-azabicyclo[3.1.0]hex-1-yl]- (CA INDEX NAME)



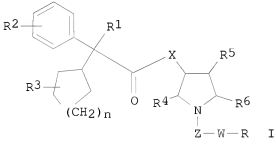

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2004:546475 CAPLUS |
| DOCUMENT NUMBER: | 141:106362 |
| TITLE: | Preparation of 1-substituted-3-pyrrolidine derivatives as muscarinic receptor antagonists |
| INVENTOR(S): | Mehta, Anita; Gupta, Jang Bahadur; Sarma, Pakala Kumara Savithru |
| PATENT ASSIGNEE(S): | Ranbaxy Laboratories Limited, India |
| SOURCE: | PCT Int. Appl., 47 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 1 |
| PATENT INFORMATION: | |

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004056767 | A1 | 20040708 | WO 2002-IB5590 | 20021223 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002347552 | A1 | 20040714 | AU 2002-347552 | 20021223 |
| EP 1583741 | A1 | 20051012 | EP 2002-783480 | 20021223 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| IN 2005DN03262 | A | 20071130 | IN 2005-DN3262 | 20050722 |
| US 20060194862 | A1 | 20060831 | US 2006-540245 | 20060207 |
| PRIORITY APPLN. INFO.: | | | WO 2002-IB5590 A | 20021223 |
| OTHER SOURCE(S): | CASREACT 141:106362; MARPAT 141:106362 | | | |

GI




I

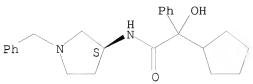
AB Title muscarinic receptor antagonists I (X = O, NH, etc.; R1 = OH, etc.; R2 = H, halo, alkyl; R3 = H, OH, etc.; R4, R5, R6 = H, alkyl; ; Z = CH2, SO2, carbonyl; W = alkylene, etc.; R = alkyl, aryl, etc.), useful for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors, are prepared The affinity of these compds. for M2 and M3 muscarinic receptor subtype was tested. For example, (3S)-1-benzylpyrrolidin-3-yl cyclopentyl(hydroxy)phenylacetate was prepared and had pKi = 6.13/7.17 for the M2 and M3 receptor subtype resp.

IT 719278-59-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 1-substituted-3-pyrrolidine derivs. as muscarinic receptor antagonists)

RN 719278-59-8 CAPLUS

CN Benzeneacetamide, α-cyclopentyl-α-hydroxy-N-[(3S)-1-(phenylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:696005 CAPLUS
DOCUMENT NUMBER: 137:232914
TITLE: Template-fixed peptidomimetics with antimicrobial activity
INVENTOR(S): Obrecht, Daniel; Robinson, John Anthony; Vrijbloed, Jan Wim
PATENT ASSIGNEE(S): Polyphor Ltd., Switz.; Universitaet Zuerich
SOURCE: PCT Int. Appl., 262 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002070547 | A1 | 20020912 | WO 2002-EP1711 | 20020218 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2439178 | A1 | 20020912 | CA 2002-2439178 | 20020218 |
| AU 2002247724 | A1 | 20020919 | AU 2002-247724 | 20020218 |
| AU 2002247724 | B2 | 20080207 | | |
| EP 1363934 | A1 | 20031126 | EP 2002-716787 | 20020218 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2002007502 | A | 20040309 | BR 2002-7502 | 20020218 |
| CN 1498225 | A | 20040519 | CN 2002-805453 | 20020218 |
| JP 2004534738 | T | 20041118 | JP 2002-569866 | 20020218 |
| US 20040171066 | A1 | 20040902 | US 2004-469060 | 20040205 |
| US 7253146 | B2 | 20070807 | | |
| HK 1064391 | A1 | 20061201 | HK 2004-107145 | 20040917 |

PRIORITY APPLN. INFO.: WO 2001-EP2072 W 20010223
WO 2002-EP1711 W 20020218

OTHER SOURCE(S): MARPAT 137:232914

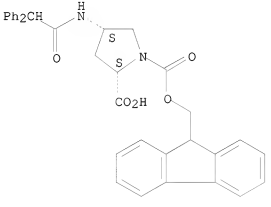
AB Template-fixed β-hairpin peptidomimetics having sequences of the type -N-Z-CO-, where Z is a chain of 8 to 16 α-amino acid residues, and their salts inhibit the growth or kill microorganisms and cancer cells. They can be used as disinfectants for foodstuffs, cosmetics, medicaments or other nutrient-containing materials or as medicaments to treat or prevent infections or diseases related to such infections and/or cancer. These β-hairpin peptidomimetics can be manufactured by a process which is based on a mixed solid- and solution phase synthetic strategy. Thus, a peptide having the sequence Arg-Leu-Tyr-Arg-D-Pro-Pro-Arg-Tyr-Tyr-Arg-Arg, in which the template is D-Pro-Pro, was synthesized by the solid-phase method and assayed for antimicrobial activity (MIC = 25 μg/mL at a concentration of 100 μg/mL in the case of Escherichia coli).

IT 458546-92-4P 458547-11-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(template-fixed peptidomimetics with antimicrobial activity)

RN 458546-92-4 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(diphenylacetyl)amino]-, 1-(9H-fluoren-9-ylmethyl) ester, (2S,4S)- (9CI) (CA INDEX NAME)

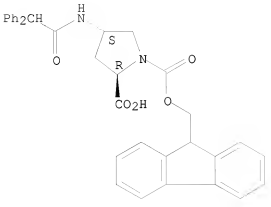
Absolute stereochemistry.



RN 458547-11-0 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 4-[(diphenylacetyl)amino]-, 1-(9H-fluoren-9-ylmethyl) ester, (2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:115088 CAPLUS
DOCUMENT NUMBER: 134:178141
TITLE: Preparation of oxoazacycloalkanes and analogs
INVENTOR(S): Hulme, Christopher; Morton, George C.; Salvino, Joseph M.; Labaudiniere, Richard F.; Mason, Helen J.; Morrissette, Mathew M.; Ma, Liang; Cherrier, Marie-Pierre
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Products, Inc., USA
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001010799 | A1 | 20010215 | WO 2000-US21257 | 20000803 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6492553 | B1 | 20021210 | US 1999-368213 | 19990804 |
| EP 1212269 | A1 | 20020612 | EP 2000-955355 | 20000803 |
| EP 1212269 | B1 | 20041027 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2003506420 | T | 20030218 | JP 2001-515272 | 20000803 |
| AT 280744 | T | 20041115 | AT 2000-955355 | 20000803 |
| ES 2230143 | T3 | 20050501 | ES 2000-955355 | 20000803 |
| HK 1046897 | A1 | 20050415 | HK 2002-108269 | 20021115 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1999-368213 | A | 19990804 |
| US 1998-73007P | P | 19980129 |
| US 1998-98404P | P | 19980831 |
| US 1998-98708P | P | 19980901 |
| US 1998-101056P | P | 19980918 |
| WO 1999-US1923 | A2 | 19990129 |
| WO 2000-US21257 | W | 20000803 |

OTHER SOURCE(S): CASREACT 134:178141; MARPAT 134:178141

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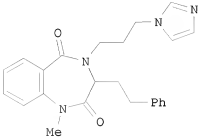


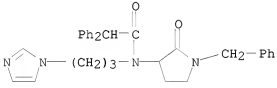
I

AB The title process comprises, e.g., Ugi condensation of N-protected anthranilic acids, amines, aldehydes, and an isocyanide followed by deprotection and cyclization. Thus, 2-(BocMeN)C6H4CO2H, imidazole-1-propanamine, PhCH2CH2CHO, and an isocyanide were combined to give title compound I.

IT 234781-55-6P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of oxoazacycloalkanes and analogs)

RN 234781-55-6 CAPLUS

CN Benzeneacetamide, N-[3-(1H-imidazol-1-yl)propyl]-N-[2-oxo-1-(phenylmethyl)-3-pyrrolidinyl]-α-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:314672 CAPLUS

DOCUMENT NUMBER: 132:334358

TITLE: Preparation of pyrrolidine compounds as antagonists of serotonin 2 receptor

INVENTOR(S): Kuroita, Takanobu; Fujio, Masakazu; Nakagawa, Haruto

PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan

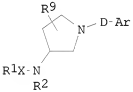
SOURCE: PCT Int. Appl., 94 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000026186 | A1 | 20000511 | WO 1999-JP6002 | 19991028 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2348879 | A1 | 20000511 | CA 1999-2348879 | 19991028 |
| AU 9963673 | A | 20000522 | AU 1999-63673 | 19991028 |
| EP 1125922 | A1 | 20010822 | EP 1999-951139 | 19991028 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| US 6468998 | B1 | 20021022 | US 2001-830718 | 20010501 |

PRIORITY APPLN. INFO.: JP 1998-311868 A 19981102
WO 1999-JP6002 W 19991028

OTHER SOURCE(S): MARPAT 132:334358
GI



I

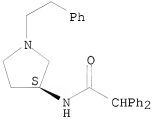
AB Described are pyrrolidine compds. represented by general formula [I; R1 = Q-Q5, etc. a proviso is given; R9 = H, C1-6 alkyl, C1-6 alkoxy, C1-6 hydroxyalkyl; X = CO, CS, NHCO, SO, SO2; R2 = H, alkyl, acyl, (un)substituted arylalkyl, (un)substituted aromatic ring, heterocyclic ring containing at least one atom selected from O, N, and S; D = C1-6 (un)substituted alkyl, alkenyl, etc], optically active isomers thereof or pharmaceutically acceptable salts of the same; and medicinal compns. containing the compds. of general formula I, optically active isomers thereof or pharmaceutically acceptable salts of the same together with pharmaceutically acceptable additives. These compds. have an antagonism to serotonin 2 receptor, a platelet aggregation inhibitory effect, a peripheral circulation improving effect and a lacrimal secretion promoting effect, which makes them useful as drugs for thromboembolism, dry eye, etc. Thus, 2-(4-fluorophenyl)ethyl p-toluenesulfonate and (S)-N-(pyrrolidin-3-yl)-1-adamantanecarboxamide were dissolved in DMF and stirred with K2CO3 at 70° for 5 h to give (S)-N-[1-[2-(4-fluorophenyl)ethyl]pyrrolidin-3-yl]-1-adamantanecarboxamide (II) which was converted into the HCl salt. II.HCl in vitro inhibited the binding of

3H-ketanserin to 5-HT2 receptor preparation from rat cerebral cortex synapse with IC50 of 0.18 nM vs. sarpogrelate. It in vitro showed IC50 of 1.9 μg/mL for inhibiting the collagen-induced rabbit blood platelet aggregation vs. 260 and 1,378 for sarpogrelate and cilostazol, resp.

IT 267643-80-1P 267643-81-2P 267643-84-5P
267643-85-6P 267643-86-7P 267643-92-5P
267643-93-6P 267644-02-0P 267644-12-2P
267644-14-4P 267644-15-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidine compds. as antagonists of serotonin 2 receptor for drugs)

RN 267643-80-1 CAPLUS
CN Benzeneacetamide, α-phenyl-N-[(3S)-1-(2-phenylethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

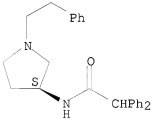



RN 267643-81-2 CAPLUS
CN Benzeneacetamide, α-phenyl-N-[(3S)-1-(2-phenylethyl)-3-pyrrolidinyl]-, ethanedioate (1:1) (CA INDEX NAME)

CM 1

CRN 267643-80-1
CMF C26 H28 N2 O

Absolute stereochemistry.




CM 2

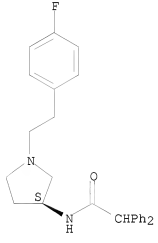
CRN 144-62-7
CMF C2 H2 O4

RN 267643-84-5 CAPLUS
CN Benzeneacetamide, N-[(3S)-1-[2-(4-fluorophenyl)ethyl]-3-pyrrolidinyl]-α-phenyl-, ethanedioate (1:1) (CA INDEX NAME)

CM 1

CRN 267643-83-4
CMF C26 H27 F N2 O

Absolute stereochemistry.

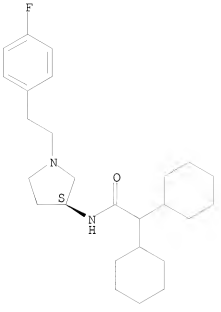


CM 2

CRN 144-62-7
CMF C2 H2 O4

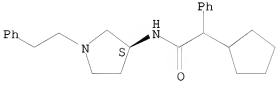
RN 267643-85-6 CAPLUS
CN Cyclohexaneacetamide, α-cyclohexyl-N-[(3S)-1-[2-(4-fluorophenyl)ethyl]-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



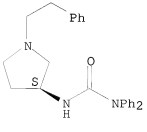
RN 267643-86-7 CAPLUS
CN Benzeneacetamide, α-cyclopentyl-N-[(3S)-1-(2-phenylethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 267643-92-5 CAPLUS
CN Urea, N,N-diphenyl-N'-[(3S)-1-(2-phenylethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

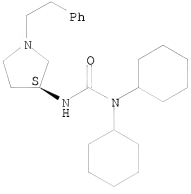
Absolute stereochemistry.



RN 267643-93-6 CAPLUS
CN Urea, N,N-dicyclohexyl-N'-[(3S)-1-(2-phenylethyl)-3-pyrrolidinyl]- (CA

INDEX NAME)

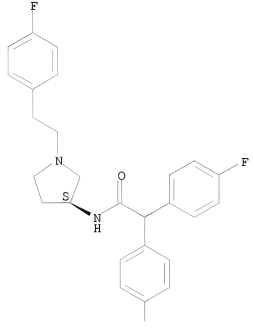
Absolute stereochemistry.




RN 267644-02-0 CAPLUS
CN Benzeneacetamide, 4-fluoro-α-(4-fluorophenyl)-N-[(3S)-1-[2-(4-fluorophenyl)ethyl]-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

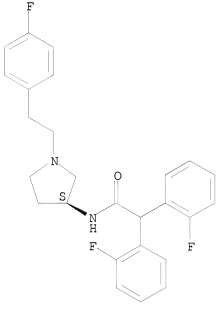


PAGE 2-A

F

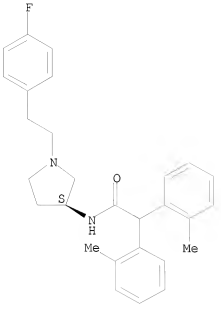
RN 267644-12-2 CAPLUS
CN Benzeneacetamide, 2-fluoro-α-(2-fluorophenyl)-N-[(3S)-1-[2-(4-fluorophenyl)ethyl]-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



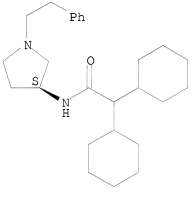
RN 267644-14-4 CAPLUS
CN Benzeneacetamide, N-[(3S)-1-[2-(4-fluorophenyl)ethyl]-3-pyrrolidinyl]-2-methyl-α-(2-methylphenyl)- (CA INDEX NAME)

Absolute stereochemistry.




RN 267644-15-5 CAPLUS
CN Cyclohexaneacetamide, α-cyclohexyl-N-[(3S)-1-(2-phenylethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

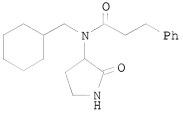
Absolute stereochemistry.



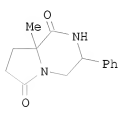

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:226851 CAPLUS
DOCUMENT NUMBER: 133:17439
TITLE: Novel applications of convertible isonitriles for the synthesis of mono and bicyclic γ-lactams via a UDC strategy
AUTHOR(S): Hulme, Christopher; Ma, Liang; Cherrier, Marie-Pierre; Romano, Joseph J.; Morton, George; Duquenne, Celine; Salvino, Joseph; Labaudiniere, Richard

CORPORATE SOURCE: New Leads Discovery, New Leads Discovery, Rhone-Poulenc Rorer Central Research, Collegeville, PA, 19426, USA
SOURCE: Tetrahedron Letters (2000), 41(12), 1883-1887
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

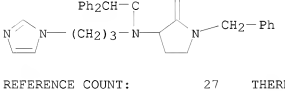



I




II

AB This communication reveals a novel application of the so-called convertible isonitriles for the solution/solid phase generation of γ-lactam analogs. Use of tethered N-BOC aldehydes, e.g., BocNHCH2CH2CHO, in the Ugi multi-component reaction (MCR), followed by BOC removal and base treatment (a "3-step, 1-pot procedure") affords γ-lactams, e.g., I, in good yield. The UDC (Ugi/De-BOC/Cyclize) strategy, coupled with a convertible isonitrile, is now feasible from all three substitution sites of the Ugi product. A conceptually novel approach, combining a bi-functional precursor with a post-condensation modification to give fused lactam-ketopiperazines, e.g., II, is also revealed.
IT 234781-55-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of γ-lactams from carboxylic acids and amines via UDC strategy using isonitriles)
RN 234781-55-6 CAPLUS
CN Benzeneacetamide, N-[3-(1H-imidazol-1-yl)propyl]-N-[2-oxo-1-(phenylmethyl)-3-pyrrolidinyl]-α-phenyl- (CA INDEX NAME)



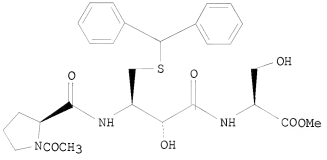

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:680120 CAPLUS
DOCUMENT NUMBER: 131:310838
TITLE: Preparation of peptides as HCV protease inhibitors

INVENTOR(S): Yamamoto, Osamu; Nakai, Eiichi; Shimizu, Yasuaki; Hara, Ryuichiro
PATENT ASSIGNEE(S): Soyaku Gijutsu Kenkyusho K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 51 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 11292840 | A | 19991026 | JP 1998-93765 | 19980406 |

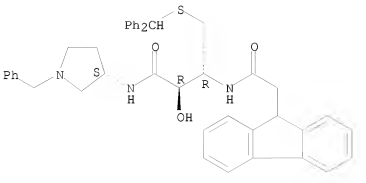
PRIORITY APPLN. INFO.: JP 1998-93765 19980406
GI



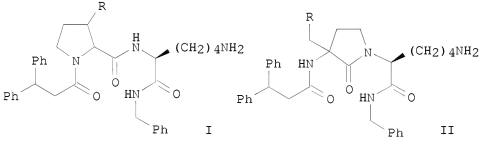

II

AB Title compds. RAN(X)CH(CH2SR1)CH(OH)COY [I; R = H, protection group of N; R1 = H, protection group of S; A = amino acid amide; X = H, fragment of amino acid; Y = amino acid, amino acid ester: such as serine and valine] and pharmaceutical acceptable salts are prepared and tested as Hepatitis C virus (HCV) protease inhibitors in treatment of hepatitis C. Thus, the title compound II was prepared
IT 247266-95-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides. as HCV protease inhibitors)
RN 247266-95-1 CAPLUS
CN 9H-Fluorene-9-acetamide, N-[(1R,2R)-1-[[(diphenylmethyl)thio]methyl]-2-hydroxy-3-oxo-3-[[(3S)-1-(phenylmethyl)-3-pyrrolidinyl]amino]propyl]- (CA INDEX NAME)

Absolute stereochemistry.



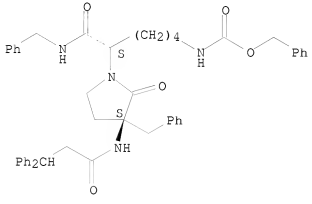
L4 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:512050 CAPLUS
DOCUMENT NUMBER: 131:286805
TITLE: Synthesis of novel proline and γ-lactam derivatives as non-peptide mimics of somatostatin / sandostatin
AUTHOR(S): Damour, Dominique; Herman, Frederic; Labaudiniere, Richard; Pantel, Guy; Vuilhorgne, Marc; Mignani, Serge
CORPORATE SOURCE: Rhone-Poulenc Rorer S.A. Centre de Recherche de Vitry-Alfortville, Vitry-sur-Seine, 94403, Fr.
SOURCE: Tetrahedron (1999), 55(33), 10135-10154
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB This paper reports the convenient synthesis of proline-based mimic I (R = Ph, 3-indolyl) and γ-lactam-based mimic II of sandostatin. In most cases, these compds. have been prepared as enantiomerically pure cis and trans-diastereoisomers.
IT 246870-33-7P 246870-36-0P 246870-41-7P
246870-42-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of novel proline- and γ-lactam-based mimics of sandostatin/somatostatin)

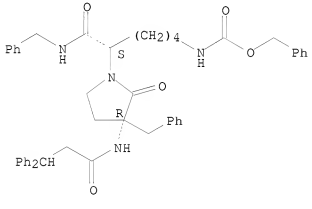
RN 246870-33-7 CAPLUS
CN Carbamic acid, [(5S)-6-oxo-5-[(3S)-2-oxo-3-[(1-oxo-3,3-diphenylpropyl)amino]-3-(phenylmethyl)-1-pyrrolidinyl]-6-[(phenylmethyl)amino]hexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



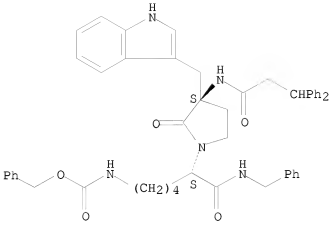
RN 246870-36-0 CAPLUS
CN Carbamic acid, [(5S)-6-oxo-5-[(3R)-2-oxo-3-[(1-oxo-3,3-diphenylpropyl)amino]-3-(phenylmethyl)-1-pyrrolidinyl]-6-[(phenylmethyl)amino]hexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



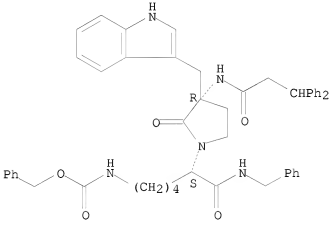
RN 246870-41-7 CAPLUS
CN Carbamic acid, [(5S)-5-[(3S)-3-(1H-indol-3-ylmethyl)-2-oxo-3-[(1-oxo-3,3-diphenylpropyl)amino]-1-pyrrolidinyl]-6-oxo-6-[(phenylmethyl)amino]hexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



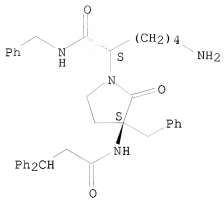
RN 246870-42-8 CAPLUS
CN Carbamic acid, [(5S)-5-[(3R)-3-(1H-indol-3-ylmethyl)-2-oxo-3-[(1-oxo-3,3-diphenylpropyl)amino]-1-pyrrolidinyl]-6-oxo-6-[(phenylmethyl)amino]hexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



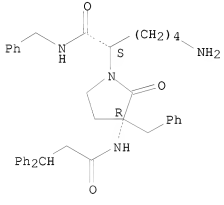
IT 246870-37-1P 246870-38-2P 246870-43-9P
246870-44-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of novel proline- and γ-lactam-based mimics of sandostatin/somatostatin)
RN 246870-37-1 CAPLUS
CN 1-Pyrrolidineacetamide, α-(4-aminobutyl)-2-oxo-3-[(1-oxo-3,3-diphenylpropyl)amino]-N,3-bis(phenylmethyl)-, (αS,3S)- (CA INDEX NAME)

Absolute stereochemistry.



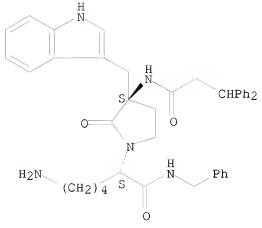
RN 246870-38-2 CAPLUS
CN 1-Pyrrolidineacetamide, α-(4-aminobutyl)-2-oxo-3-[(1-oxo-3,3-diphenylpropyl)amino]-N,3-bis(phenylmethyl)-, (αS,3R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 246870-43-9 CAPLUS
CN 1-Pyrrolidineacetamide, α-(4-aminobutyl)-3-(1H-indol-3-ylmethyl)-2-oxo-3-[(1-oxo-3,3-diphenylpropyl)amino]-N-(phenylmethyl)-, monohydrochloride, (αS,3S)- (9CI) (CA INDEX NAME)

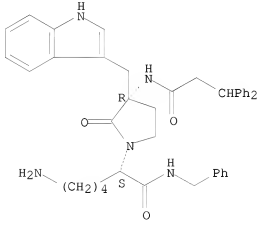
Absolute stereochemistry.



● HCl

RN 246870-44-0 CAPLUS
CN 1-Pyrrolidineacetamide, α-(4-aminobutyl)-3-(1H-indol-3-ylmethyl)-2-oxo-3-[(1-oxo-3,3-diphenylpropyl)amino]-N-(phenylmethyl)-, monohydrochloride, (αS,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:495272 CAPLUS

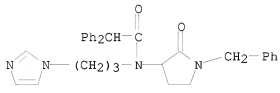
DOCUMENT NUMBER: 131:130011
TITLE: Preparation of N-acyl-2-aminoacetamides and cyclization products thereof.
INVENTOR(S): Hulme, Christopher; Morton, George C.; Salvino, Joseph M.; Labaudiniere, Richard F.; Mason, Helen J.; Morrissette, Matthew M.; Ma, Liang; Cherrier, Marie-Pierre
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9938844 | A1 | 19990805 | WO 1999-US1923 | 19990129 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2318601 | A1 | 19990805 | CA 1999-2318601 | 19990129 |
| AU 9924821 | A | 19990816 | AU 1999-24821 | 19990129 |
| AU 747987 | B2 | 20020530 | | |
| ZA 9900729 | A | 20000110 | ZA 1999-729 | 19990129 |
| EP 1051397 | A1 | 20001115 | EP 1999-904421 | 19990129 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO | | | | |
| BR 9908207 | A | 20001128 | BR 1999-8207 | 19990129 |
| JP 2002501944 | T | 20020122 | JP 2000-530081 | 19990129 |
| HU 2001001329 | A2 | 20020328 | HU 2001-1329 | 19990129 |
| HU 2001001329 | A3 | 20020729 | | |
| AP 1462 | A | 20050930 | AP 2000-1864 | 19990129 |
| W: GH, GM, KE, LS, MW, SD, SZ, UG, ZW | | | | |
| US 6492553 | B1 | 20021210 | US 1999-368213 | 19990804 |
| NO 2000003792 | A | 20000927 | NO 2000-3792 | 20000724 |
| NO 324067 | B1 | 20070806 | | |
| MX 2000PA07555 | A | 20010219 | MX 2000-PA7555 | 20000801 |
| BG 104724 | A | 20010330 | BG 2000-104724 | 20000829 |
| BG 65057 | B1 | 20070131 | | |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 1998-73007P | A2 | 19980129 |
| | US 1998-98404P | A2 | 19980831 |
| | US 1998-98708P | A2 | 19980901 |
| | US 1998-101056P | A2 | 19980918 |
| | WO 1999-US1923 | W | 19990129 |

OTHER SOURCE(S): MARPAT 131:130011
AB RaRbNCRcaRcbRd Ra = RaaCO; Dd = CONHRda; Raa, Rb, Rca, Rcb = H, (substituted) aliphatyl, aryl; Rda = (substituted) aliphatyl, aryl; with provisos were prepared by reaction of RcaCORcb with RbNH2, RaCO2H, and NCRda. Title compds. may be prepared on a isocyanide resin and deprotected/cyclized to give 1,4-benzodiazepine-2,5-diones, diketopiperazines, ketopiperazines, lactams, 1,4-benzodiazapines, and

dihydroquinoxalinones.
IT 234781-55-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of N-acyl-2-aminoacetamides and cyclization products thereof)
RN 234781-55-6 CAPLUS
CN Benzeneacetamide, N-[3-(1H-imidazol-1-yl)propyl]-N-[2-oxo-1-(phenylmethyl)-3-pyrrolidinyl]-α-phenyl- (CA INDEX NAME)



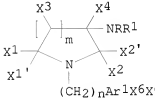
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:134849 CAPLUS
DOCUMENT NUMBER: 126:157509
TITLE: Preparation of substituted (sulfinic acid, sulfonic acid, sulfonylamino or sulfinylamino) N-[(aminoiminomethyl)phenylalkyl]azaheterocyclylamide compounds as Factor Xa inhibitors
INVENTOR(S): Ewing, William R.; Becker, Michael R.; Pauls, Henry W.; Cheney, Daniel L.; Mason, Jonathan Stephen; Spada, Alfred P.; Choi-Sledeski, Yong Mi
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 272 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9640679 | A1 | 19961219 | WO 1996-US9816 | 19960607 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN | | | | |
| US 5612353 | A | 19970318 | US 1995-481024 | 19950607 |
| CA 2223403 | A1 | 19961219 | CA 1996-2223403 | 19960607 |
| CA 2223403 | C | 20020423 | | |
| AU 9661669 | A | 19961230 | AU 1996-61669 | 19960607 |
| AU 714319 | B2 | 20000106 | | |
| EP 853618 | A1 | 19980722 | EP 1996-919298 | 19960607 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LV, FI | | | | |
| CN 1190395 | A | 19980812 | CN 1996-194489 | 19960607 |
| JP 11507368 | T | 19990629 | JP 1996-502029 | 19960607 |

| | | | | | |
|---|---|---|---|---|---|
| | BR 9608405 | A | 19990824 | BR 1996-8405 | 19960607 |
| | AP 799 | A | 20000119 | AP 1997-1144 | 19960607 |
| | NO 9705762 | A | 19980206 | NO 1997-5762 | 19971208 |
| | NO 310457 | B1 | 20010709 | | |
| | BG 63628 | B1 | 20020731 | BG 1998-102162 | 19980106 |
| | US 6034093 | A | 20000307 | US 1998-130336 | 19980806 |
| PRIORITY APPLN. INFO.: | | | | US 1995-481024 | A 19950607 |
| | | | | WO 1996-US9816 | W 19960607 |
| | | | | US 1996-761414 | A2 19961206 |
| | | | | US 1997-976034 | A2 19971121 |
| | | | | WO 1997-US22414 | A2 19971201 |

OTHER SOURCE(S): MARPAT 126:157509
GI




(CH2)nAr1X6X6'CX5X5'NHR2 I

AB About 165 title compds. I [R = H, alkyl, aralkyl, hydroxyalkyl; R1 = H, R3S(O)p, R3R4NS(O)p; R2 = H, alkyl,aralkyl; R3 = alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl; RR3 = 5-7 membered ring; R4 = alkyl, cycloalkyl, aryl, heteroaryl; R3R4N = 4-7 membered heterocyclyl; X1, X1' = H, alkyl, aryl, aralkyl, etc.; X1X1' = oxo; X2, X2' = H; X2X2' = O; X4 = H, alkyl, aralkyl, hydroxyalkyl; X5, X5' = H; X5X5' = NR5; R5 = H, R6O2C, R6O, cyano, R6CO, alkyl, NO2, etc.; X6, X6' = H, R7R8N, R9O, R7R8NCO, R7R8NSO2, etc.; R7, R8 = H, alkyl; R9 = H, alkyl, acyl, etc.; m = 0-3; n = 1-3; p = 1, 2] were prepared I are inhibitors of the activity of Factor Xa. E.g., 7-hydroxynaphthalene-2-sulfonic acid Na salt was methylated with di-Me sulfate/NaOH, treated with phosphorus oxychloride/PCl5, and reacted with 3-(3S-amino-2-oxopyrrolidin-1-ylmethyl)benzonitrile hydrochloride to give 7-hydroxynaphthalene-2-sulfonic acid {1-[3-(aminoiminomethyl)benzyl]-2-oxopyrrolidin-3(S)-yl}amide trifluoroacetate. In a test of Factor Xa inhibition, the last had a Ki value of 35 nM.

IT 186548-46-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted (sulfinic acid, sulfonic acid, sulfonylamino or sulfinylamino) N-[(aminoiminomethyl)phenylalkyl]azaheterocyclylamide compds. as Factor Xa inhibitors)

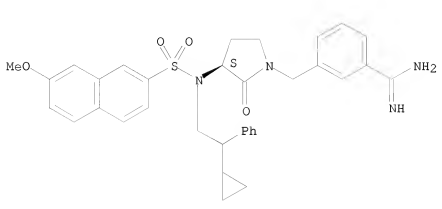
RN 186548-46-9 CAPLUS

CN Benzenecarboximidamide, 3-[[3-[(2-cyclopropyl-2-phenylethyl)[(7-methoxy-2-naphthalenyl)sulfonyl]amino]-2-oxo-1-pyrrolidinyl]methyl]-, (3S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 186548-45-8
CMF C34 H36 N4 O4 S

Absolute stereochemistry.

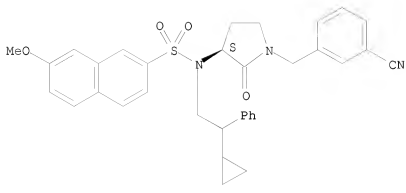


CM 2

CRN 76-05-1
CMF C2 H F3 O2

IT 186551-46-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted (sulfinic acid, sulfonic acid, sulfonylamino or sulfinylamino) N-[(aminoiminomethyl)phenylalkyl]azaheterocyclylamide compds. as Factor Xa inhibitors)
RN 186551-46-2 CAPLUS
CN 2-Naphthalenesulfonamide, N-[1-[(3-cyanophenyl)methyl]-2-oxo-3-pyrrolidinyl]-N-(2-cyclopropyl-2-phenylethyl)-7-methoxy-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




L4 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:94071 CAPLUS
DOCUMENT NUMBER: 126:104431
TITLE: Preparation of heterocyclic dipeptide derivatives which promote release of growth hormone
INVENTOR(S): Carpino, Philip A.; Jardine DaSilva, Paul A.; Lefker, Bruce A.; Ragan, John A.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9638471 | A1 | 19961205 | WO 1995-IB410 | 19950529 |
| W: CA, FI, JP, MX, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2220055 | A1 | 19961205 | CA 1995-2220055 | 19950529 |
| CA 2220055 | C | 20010424 | | |
| EP 828754 | A1 | 19980318 | EP 1995-918123 | 19950529 |
| EP 828754 | B1 | 20050202 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE | | | | |
| JP 10510511 | T | 19981013 | JP 1995-511175 | 19950529 |
| JP 3133073 | B2 | 20010205 | JP 1996-511175 | 19950529 |
| AT 288444 | T | 20050215 | AT 1995-918123 | 19950529 |
| ES 2235171 | T3 | 20050701 | ES 1995-918123 | 19950529 |
| NO 9602162 | A | 19961202 | NO 1996-2162 | 19960528 |
| AU 9654554 | A | 19961212 | AU 1996-54554 | 19960528 |
| CN 1143647 | A | 19970226 | CN 1996-107637 | 19960528 |
| US 5936089 | A | 19990810 | US 1997-973268 | 19971126 |
| FI 9704368 | A | 19971128 | FI 1997-4368 | 19971128 |

PRIORITY APPLN. INFO.: WO 1995-IB333 A 19950508
WO 1995-IB410 W 19950529

OTHER SOURCE(S): MARPAT 126:104431
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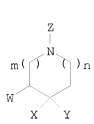

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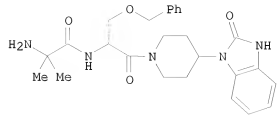


II

AB Title compds. I [Z = COCR1R2cLCOANR4R5; L = NR6, O, CH2; W = H; W and X = benzo fusion substituted with 0-3 R3a, TR3b, or R12; Y = H, C1-6 alkyl, C4-10 cycloalkyl, aryl-K, phenyl-(C1-6alkyl)-K, thienyl-(C1-6 alkyl)-K substituted with 0-3 R3a, R3b, or R12; K = bond, O, S(O)m, NR2a; X = OR2, R50MN(Aryl), R8R9NCO, R2bO2C, (un)substituted carbo- or heterobicyclic ring; R1 = (un)substituted C1-10 alkyl, aryl, etc.; R2c = H, C1-6 alkyl, C3-7 cycloalkyl; CR1R3c = (un)substituted C3-8 ring; R2 = H, C1-6 alkyl, C3-7 cycloalkyl; R2a = H, C1-6 alkyl; R2b = H, C1-8 alkyl, C1-8 halogenated alkyl, C3-8 cycloalkyl, alkylaryl, aryl; R3a, R12 = independently H, halo, Me, OMe, CF3; T = bond, phenylene, 5- or 6-membered heterocycle containing 1-3 hetero atoms; R3b = H, CONR8R9, SO2R8R9, CO2H, CO2(C1-6 alkyl), NR2SO2R9, NR2CONR8R9, NR2SO2NR8R9, NR2COR9, imidazolyl, thiazolyl, tetrazolyl; R4, R5 = independently H, (un)substituted C1-6 alkyl; R6 = H, C1-6 alkyl; R6CR2c = C3-8 ring; R50 = (un)substituted morpholino, piperazino, C3-7 cycloalkyl, C1-6 alkyl; M = CO, SO2; A = bond, Z1(CH2)xCR7R7a(CH2)y; Z1 = NR2, O, bond; R7, R7a = independently H, CF3, Ph, (un)substituted C1-6 alkyl; R8 = H, (un)substituted C1-6 alkyl; R9 = H, (un)substituted C1-6 alkyl, Ph, thiazolyl, imidazolyl, furyl, thienyl], are growth hormone releasing peptide mimics. Heterocyclic dipeptide derivs. I are useful for the treatment and prevention of osteoporosis (no data). Thus, condensation of Boc-D-Ser(CH2Ph)-OH (Boc = Me3CO2C) with 4-(2-oxo-1-benzimidazolinyl)piperidine, followed by deprotection, coupling with BocNHCMe2CO2H, and deprotection with HCl gave dipeptide amide salt II.

IT 185056-17-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of growth hormone-releasing dipeptides)

RN 185056-17-1 CAPLUS

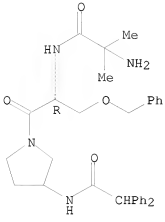
CN Benzeneacetamide, N-[1-[2-methylalanyl-O-(phenylmethyl)-D-seryl]-3-pyrrolidinyl]-α-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 185056-16-0

CMF C32 H38 N4 O4

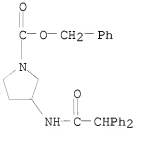
Absolute stereochemistry.



CM 2

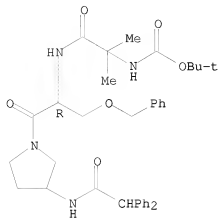
CRN 76-05-1
CMF C2 H F3 O2

IT 185057-88-9P 185057-90-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of growth hormone-releasing dipeptides)
RN 185057-88-9 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-[(diphenylacetyl)amino]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 185057-90-3 CAPLUS
CN Carbamic acid, [2-[[2-[3-[(diphenylacetyl)amino]-1-pyrrolidinyl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]amino]-1,1-dimethyl-2-oxoethyl]-, 1,1-dimethylethyl ester, (R)- (9CI) (CA INDEX NAME)

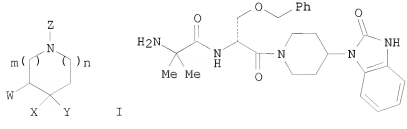
Absolute stereochemistry.



L4 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:26293 CAPLUS
DOCUMENT NUMBER: 126:60362
TITLE: Preparation of heterocyclic dipeptide derivatives which promote release of growth hormone
INVENTOR(S): Carpino, Philip A.; Jardine DaSilva, Paul A.; Lefker, Bruce A.; Ragan, John A.
PATENT ASSIGNEE(S): Pfizer, Inc., USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9635713 | A1 | 19961114 | WO 1995-IB333 | 19950508 |
| W: CA, FI, JP, MX, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9654554 | A | 19961212 | AU 1996-54554 | 19960528 |
| PRIORITY APPLN. INFO.: | | | WO 1995-IB333 A | 19950508 |
| | | | WO 1995-IB410 A | 19950529 |

OTHER SOURCE(S): MARPAT 126:60362
GI



I II

AB Title compds. I [Z = COCR1R2cLCOANR4R5; L = NR6, O, CH2; W = H; W and X = benzo fusion optionally substituted with 1-3 R3a, TR3b, or R12; Y = H, C1-6 alkyl, C3-10 cycloalkyl, aryl optionally substituted with 1-3 R3a, R3b, or R12; X = OR2, R50MN(Aryl), R8R9NCO, R2bO2C, optionally substituted carbobicyclic or heterobicyclic ring; R1 = optionally substituted C1-10 alkyl, aryl, etc.; R2c = H, C1-6 alkyl, C3-7 cycloalkyl; CR1R3c = optionally substituted C3-8 ring; R2 = H, C1-6 alkyl, C3-7 cycloalkyl; R2a = H, C1-6 alkyl; R2b = H, C1-8 alkyl, C1-8 halogenated alkyl, C3-8 cycloalkyl, alkylaryl, aryl; R3a, R12 = independently H, halo, Me, OMe, CF3; T = bond, phenylene, 5- or 6-membered heterocycle containing 1-3 hetero atoms; R3b = H, CONR8R9, SO2R8R9, CO2H, CO2(C1-6 alkyl), NR2SO2R9, NR2CONR8R9, NR2SO2NR8R9, NR2COR9, imidazolyl, thiazolyl, tetrazolyl; R4, R5 = independently H, optionally substituted C1-6 alkyl; R6 = H, C1-6 alkyl; R6CR2c = C3-8 ring; R50 = optionally substituted morpholino, piperazino, C3-7 cycloalkyl, C1-6 alkyl; M = CO, SO2; A = bond, Z1(CH2)xCR7R7a(CH2)y; Z1 = NR2, O, bond; R7, R7a = independently H, CF3, Ph, optionally substituted C1-6 alkyl; R8 = H, optionally substituted C1-6 alkyl; R9 = H, optionally substituted C1-6 alkyl, Ph, thiazolyl, imidazolyl, furyl, thienyl], are growth hormone releasing peptide mimics. Heterocyclic dipeptide derivs. I are useful for the treatment and prevention of osteoporosis. Thus, condensation of Boc-D-Ser(CH2Ph)-OH (Boc = Me3CO2C) with 4-(2-oxo-1-benzimidazolinyl)piperidine, followed by deprotection, coupling with BocNHCMe2CO2H, and deprotection with HCl gave dipeptide amide salt II.

IT 185056-17-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and growth hormone releasing activity of heterocyclic dipeptide derivs.)

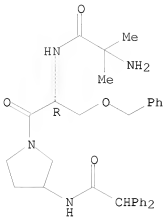
RN 185056-17-1 CAPLUS

CN Benzeneacetamide, N-[1-[2-methylalanyl-O-(phenylmethyl)-D-seryl]-3-pyrrolidinyl]-α-phenyl-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 185056-16-0
CMF C32 H38 N4 O4

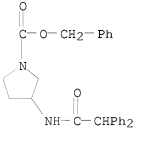
Absolute stereochemistry.



CM 2

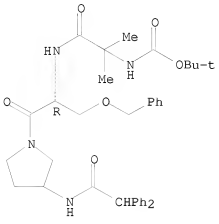
CRN 76-05-1
CMF C2 H F3 O2

IT 185057-88-9P 185057-90-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and growth hormone releasing activity of heterocyclic dipeptide derivs.)
RN 185057-88-9 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-[(diphenylacetyl)amino]-, phenylmethyl ester (9CI) (CA INDEX NAME)

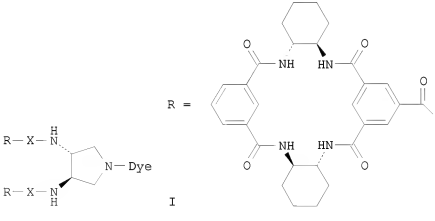


RN 185057-90-3 CAPLUS
CN Carbamic acid, [2-[[2-[3-[(diphenylacetyl)amino]-1-pyrrolidinyl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]amino]-1,1-dimethyl-2-oxoethyl]-, 1,1-dimethylethyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:501342 CAPLUS
DOCUMENT NUMBER: 125:196315
TITLE: Sequence-Selective Receptors of Peptides. A Simple Molecular Design for Construction of Large Combinatorial Libraries of Receptors
AUTHOR(S): Shao, Yuefei; Still, W. Clark
CORPORATE SOURCE: Department of Chemistry, Columbia University, New York, NY, 10027, USA
SOURCE: Journal of Organic Chemistry (1996), 61(18), 6086-6087
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB A series of synthetic receptor mols. having the general structure I [Dye =

disperse red; X = D-Phe, L-Phe, D-Asn, L-Asn, D-Asn(CPh3), L-Asn(CPh3), D-Pro, L-Pro, D-Hyp, L-Hyp] were prepared and their binding properties for a wide range of peptides were determined Receptors such as I have the useful feature that they may be prepared by combinatorial synthesis using five combinatorial steps and are thus readily available in high diversity. In this work it is shown that receptors I bind certain tripeptides sequence-selectively in organic solvents and that the particular sequences bound depend sensitively on the nature of X and its chirality. These findings indicate that receptor libraries based on I are likely to have highly selective binding properties for a wide range of specific peptidic substrates.

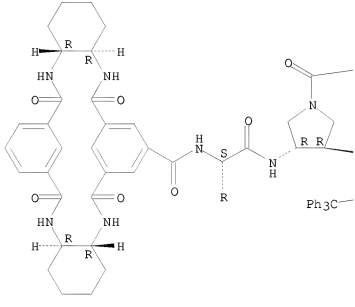
IT 180570-75-6P 180684-03-1P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(simple mol. design for construction of large combinatorial peptide receptor libraries)

RN 180570-75-6 CAPLUS

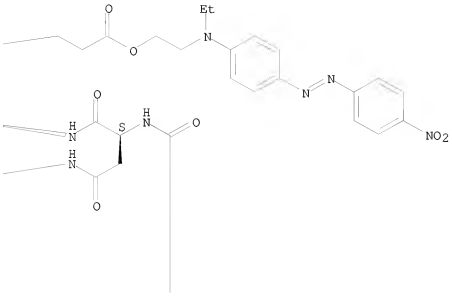
CN 1-Pyrrolidinebutanoic acid, 3,4-bis[[2-[[(1,2,3,4,4a,5,6,12,13,13a,14,15,16,17,17a,18,19,25,26,26a-eicosahydro-6,12,19,25-tetraoxo-7,11:20,24-dimethenodibenzo[b,m][1,4,12,15]tetraazacyclodocosin-9-yl)carbonyl]amino]-1,4-dioxo-4-[(triphenylmethyl)amino]butyl]amino]-γ-oxo-, 2-[ethyl[4-[(4-nitrophenyl)azo]phenyl]amino]ethyl ester, [4aR-[4aR*,9[S*[3R*,4R*[S*(4aR*,13aR*,17aR*,26aR*)]]],13aR*,17aR*,26aR*]]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

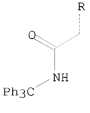
PAGE 1-A



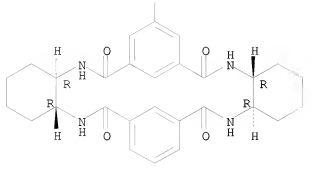
PAGE 1-B



PAGE 2-A



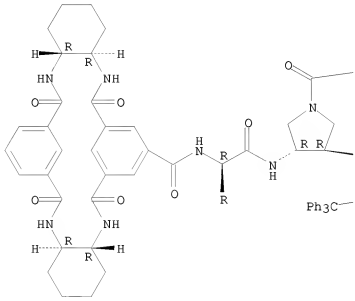
PAGE 2-B



RN 180684-03-1 CAPLUS
CN 1-Pyrrolidinebutanoic acid, 3,4-bis[[2-[[(1,2,3,4,4a,5,6,12,13,13a,14,15,16,17,17a,18,19,25,26,26a-eicosahydro-6,12,19,25-tetraoxo-7,11:20,24-dimethenodibenzo[b,m][1,4,12,15]tetraazacyclododecosin-9-yl)carbonyl]amino]-1,4-dioxo-4-[(triphenylmethyl)amino]butyl]amino]-γ-oxo-, 2-[ethyl[4-[(4-nitrophenyl)azo]phenyl]amino]ethyl ester, [4aR-[4aR*,9[R*[3R*,4R*[R*(4aR*,13aR*,17aR*,26aR*)]]],13aR*,17aR*,26aR*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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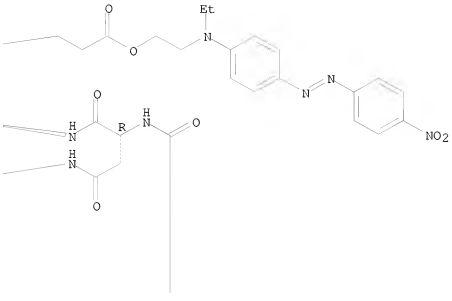


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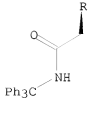

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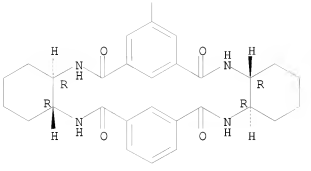
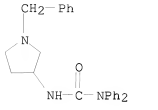


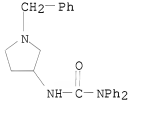
L4 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1969:68143 CAPLUS
DOCUMENT NUMBER: 70:68143
ORIGINAL REFERENCE NO.: 70:12733a,12736a
TITLE: 3-Ureidopyrrolidines
INVENTOR(S): Helsley, Grover C.
PATENT ASSIGNEE(S): A. H. Robins Co., Inc.
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3424762 | A | 19690128 | US 1966-532125 | 19660307 |
| GB 1172034 | A | 19691126 | GB 1967-1172034 | 19670307 |

PRIORITY APPLN. INFO.: US 1966-532125 A 19660307
GI For diagram(s), see printed CA Issue.
AB 1-(3-Pyrrolidinyl)-3-substituted ureas (I) are prepared which have analgetic, central nervous system, and psychopharmacologic activity. Thus, to 15 g. Na2CO3 in 100 ml. CHCl3 was added 17.6 g. 3-amino-1-benzylpyrrolidine and 23.2 g. ClCONPh2, the mixture stirred 24 hrs. at room temperature and worked up to yield 25 g. I (R = CH2Ph, R1 = H, R2 =
R3 = Ph) (II), m. 90-2° (isooctane-C6H6). The following I were similarly prepared (R, R1, R2, R3, m.p. base, and m.p. fumarate given). iso-Pr, H, Ph, Ph, -, 178-9° (iso-Pr2O); Ph, H, Ph, Ph, 167-9° (C6H6-isooctane), -; Me, H, Ph, cyclopentyl, -, 117.5-19° (iso-Pr2O). Hydrogenation of 18.6 g. II in 200 ml. 95% EtOH and 10 ml. 12N HCl over 10 g. 10% Pd on C at 60° afforded 9 g. I (R = R1 = H, R2 = R3 = Ph), m. 208-9°.
IT 19985-26-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 19985-26-3 CAPLUS
CN Urea, 3-(1-benzyl-3-pyrrolidinyl)-1,1-diphenyl- (8CI) (CA INDEX NAME)



L4 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1968:506397 CAPLUS
DOCUMENT NUMBER: 69:106397
ORIGINAL REFERENCE NO.: 69:19915a,19918a
TITLE: Synthesis and biological activity of some 1-substituted 3-pyrrolidinylureas
AUTHOR(S): Helsley, Grover C.; Franko, Bernard V.; Welstead, William J.; Lunsford, Carl D.
CORPORATE SOURCE: Res. Lab., A. H. Robins Co., Inc., Richmond, VA, USA
SOURCE: Journal of Medicinal Chemistry (1968), 11(5), 1034-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB A series of 1-substituted 3-pyrrolidinylureas (I) was synthesized and evaluated for pharmacol. activity. Some of the activities observed were central nervous system depressant, antiarrhythmic, local anesthetic, and hypoglycemic.
IT 19985-26-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 19985-26-3 CAPLUS
CN Urea, 3-(1-benzyl-3-pyrrolidinyl)-1,1-diphenyl- (8CI) (CA INDEX NAME)



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FULL ESTIMATED COST 131.28 309.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE -19.20 -19.20

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 12:25:45 ON 19 MAY 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAJRK1626

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 13:06:10 ON 19 MAY 2008
FILE 'CAPLUS' ENTERED AT 13:06:10 ON 19 MAY 2008
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 131.28 | 309.85 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -19.20 | -19.20 |

=> file reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
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| FULL ESTIMATED COST | 131.28 | 309.85 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -19.20 | -19.20 |

FILE 'REGISTRY' ENTERED AT 13:06:18 ON 19 MAY 2008
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DICTIONARY FILE UPDATES: 18 MAY 2008 HIGHEST RN 1021422-05-8

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http://www.cas.org/support/stngen/stndoc/properties.html

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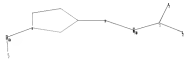

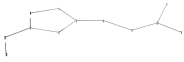

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6 7 8 9 10 11 12
ring nodes :
1 2 3 4 5
chain bonds :
1-6 3-11 6-7 7-8 8-9 8-10 11-12
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 1-6 2-3 3-4 3-11 4-5 6-7 7-8 8-9 8-10 11-12

G1:C,N

G2:Cb,Cy,Hy

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:Atom 10:Atom
11:CLASS 12:Atom

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L5              STR
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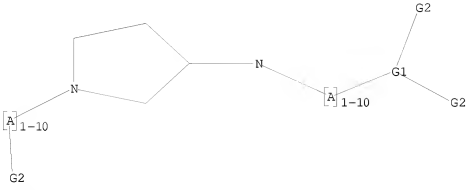


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G1 C,N
G2 Cb,Cy,Hy


Structure attributes must be viewed using STN Express query preparation.


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SAMPLE SCREEN SEARCH COMPLETED -    14580 TO ITERATE

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INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       284367 TO   298833
PROJECTED ANSWERS:               0 TO        0

L6            0 SEA SSS SAM L5

=> 15 full
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FULL SCREEN SEARCH COMPLETED -   289339 TO ITERATE

100.0% PROCESSED   289339 ITERATIONS                           106 ANSWERS
SEARCH TIME: 00.00.04

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=> l7 not l3
L8          16 L7 NOT L3

=> file caplus
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|---|---|---|
| FULL ESTIMATED COST | 178.36 | 488.21 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | 0.00 | -19.20 |

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FILE COVERS 1907 - 19 May 2008 VOL 148 ISS 21
FILE LAST UPDATED: 18 May 2008 (20080518/ED)

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=> 18
L9 8 L8

=> d ibib abs hitstr 1-8

L9 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1114104 CAPLUS
DOCUMENT NUMBER: 147:427240
TITLE: Preparation of azabicyclo[2.2.1]heptyl compounds as muscarinic receptor antagonists for treating respiratory, urinary, and gastrointestinal disorders
INVENTOR(S): Kumar, Naresh; Cliffe, Ian Anthony; Salman, Mohammad; Palle, Venkata P.; Kaur, Kirandeep; Shejul, Yogesh D.; Chugh, Anita; Gupta, Suman; Ray, Abhijit; Malhotra, Shivani; Shirumalla, Raj Kumar
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

WO 2007110782 A1 20071004 WO 2007-IB50003 20070102
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.: IN 2005-DE3522 A 20051230
OTHER SOURCE(S): CASREACT 147:427240; MARPAT 147:427240
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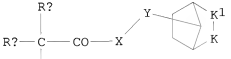


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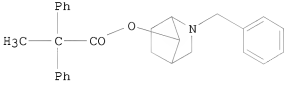
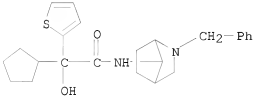



II

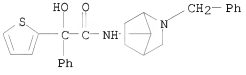
AB This present invention generally relates to muscarinic receptor antagonists of general formula I (wherein K is -CH2 and K1 is -NR1 or K1 is -CH2 and K is -NR1 (wherein R1 is H, alkyl, aryl, etc.); Y is alkylene or a single bond; X is O, S or -NR5 (wherein R5 is H, alkyl, etc.); Ra is OH, alkoxy, alkyl or H; Rb and Rc are alkyl, alkenyl, alkynyl, etc.) which are useful, among other uses, for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors. The invention also relates to the process for the preparation of disclosed compds., pharmaceutical compns. containing the disclosed compds., and the methods for treating diseases mediated through muscarinic receptors. Example compound II was prepared by reacting 2,2-diphenylpropanoic acid and 2-benzyl-7-bromo-2-azabicyclo[2.2.1]heptane. In radioligand binding assays, II had Ki values for rat M2 and M3 receptors in the range 2 - >500 nM.

IT 951393-94-5P, N-(2-Benzyl-2-azabicyclo[2.2.1]hept-7-yl)-2-cyclopentyl-2-hydroxy-2-(2-thienyl)acetamide 951393-95-6P, N-(2-Benzyl-2-azabicyclo[2.2.1]hept-7-yl)-2-hydroxy-2-phenyl-2-(2-

thienyl)acetamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of azabicyclo[2.2.1]heptyl compds. as muscarinic receptor antagonists for treating respiratory, urinary, and gastrointestinal disorders)
RN 951393-94-5 CAPLUS
CN 2-Thiopheneacetamide, α-cyclopentyl-α-hydroxy-N-[2-(phenylmethyl)-2-azabicyclo[2.2.1]hept-7-yl]- (CA INDEX NAME)



RN 951393-95-6 CAPLUS
CN 2-Thiopheneacetamide, α-hydroxy-α-phenyl-N-[2-(phenylmethyl)-2-azabicyclo[2.2.1]hept-7-yl]- (CA INDEX NAME)

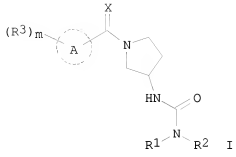


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:708222 CAPLUS
DOCUMENT NUMBER: 145:145752
TITLE: Preparation of N-(N-heterocyclylcarbonylpyrrolidin-3-yl)urea urea derivatives having antiangiogenic activity
INVENTOR(S): Haviv, Fortuna; Bradley, Michael F.; Sauer, Daryl R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 20060160806 | A1 | 20060720 | US 2004-961362 | 20041008 |
| PRIORITY APPLN. INFO.: | | | US 2003-509949P P | 20031009 |
| OTHER SOURCE(S): | MARPAT 145:145752 | | | |

GI



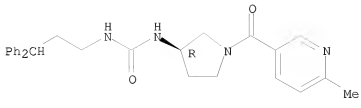
AB Compds. having the formula (I) or therapeutically acceptable salts thereof [A = pyridazinyl, pyridinyl, pyridine N-oxide, pyrimidinyl, indol-3-yl, pyrazol-4-yl, pyrazinyl, isoxazol-4-yl triazinyl; R1, R2 = H, alkenyl, alkoxy, alkoxyalkyl, alkyl, alkynyl, aryl, arylalkyl, cyanoalkyl, cycloalkyl, (cycloalkyl)alkyl, haloalkyl, heterocyclyl, heterocyclylalkyl, hydroxyalkyl, (NRARB)alkyl, (NRARB)carbonyl; or NR1R2 together forms an (un)substituted five- to seven-membered ring containing zero or one addnl. heteroatom selected; R3 = alkenyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylsulfanyl, aryl, arylalkyl, aryloxy, cyano, cyanoalkyl, cycloalkyl, (cycloalkyl)alkyl, halo, haloalkyl, heterocycle, hydroxy, hydroxyalkyl, nitro; X = O, S; m = 0-4; RA, RB = H, alkenyl, alkoxyalkyl, alkyl, alkynyl, alkylcarbonyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, heterocyclyl, heterocyclylalkyl, and hydroxyalkyl] are prepared These compds. are angiogenesis inhibitors and useful for treating conditions which arise from or are exacerbated by angiogenesis, e.g. cancer. Thus, a mixture of (3R)-1-[(6-methylpyridin-3-yl)carbonyl]pyrrolidin-3-amine bis-trifluoroacetate (0.433 g, 1.0 mmol) and Et3N (0.418 mL, 3.0 mmol) in methylene chloride (5 mL) was treated carbonyldiimidazole > (0.178 g, 1.1 mmol) and stirred for 5 h at room temperature, followed by adding pyrrolidine (3.0 mmol). The reaction mixture was
stirred for addnl. 4 h to give, N-[(3R)-1-[(6-methyl-3-pyridinyl)carbonyl]-3-pyrrolidinyl]-1-pyrrolidinecarboxamide hydrochloride (II). II at 0.1 nM inhibited 98% human microvascular endothelial cell (HMVEC) migration.

IT 850212-49-6P, N-(3,3-Diphenylpropyl)-N'-[(3R)-1-[(6-methyl-3-pyridinyl)carbonyl]-3-pyrrolidinyl]urea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (pyrrolidin-3-yl)urea ureas derivs. as angiogenesis inhibitors)

RN 850212-49-6 CAPLUS

CN Urea, N-(3,3-diphenylpropyl)-N'-[(3R)-1-[(6-methyl-3-pyridinyl)carbonyl]-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.




L9 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:672888 CAPLUS
DOCUMENT NUMBER: 143:172750
TITLE: Preparation of 3-aminopyrrolidine useful as N-type calcium channel blockers
INVENTOR(S): Pajouhesh, Hassan; Pajouhesh, Hossein; Ding, Yanbing; Snutch, Terrance P.
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 41 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 20050165065 | A1 | 20050728 | US 2004-763974 | 20040122 |
| AU 2005206226 | A1 | 20050804 | AU 2005-206226 | 20050121 |
| CA 2553773 | A1 | 20050804 | CA 2005-2553773 | 20050121 |
| WO 2005070919 | A1 | 20050804 | WO 2005-CA73 | 20050121 |
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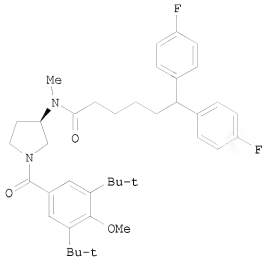
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1718633 | A1 | 20061108 | EP 2005-700289 | 20050121 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS | | | | |
| CN 1976920 | A | 20070606 | CN 2005-80006161 | 20050121 |
| BR 2005007054 | A | 20070612 | BR 2005-7054 | 20050121 |
| JP 2007518742 | T | 20070712 | JP 2006-549809 | 20050121 |
| IN 2006KN02111 | A | 20070518 | IN 2006-KN2111 | 20060726 |

PRIORITY APPLN. INFO.: US 2004-763974 A 20040122
WO 2005-CA73 W 20050121
OTHER SOURCE(S): CASREACT 143:172750; MARPAT 143:172750
GI




I

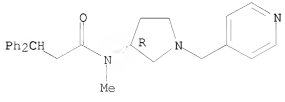
AB Title compds. I, II; X1 = N, CR3; W = L2A3, X1A1A2; L1, L2 = (substituted) alkylene, alkenylene optionally interrupted by N, O, S; A1, A2, A3 = (fused) (substituted) 6-7 membered (hetero)aliphatyl, (hetero)aryl; R1, R2 = noninterfering substituent; R3 = H, noninterfering substituent; n = 0-3; [with a proviso], were prepared The invention compds. generally contain ≥1 benzhydryl moiety, and are useful in treating conditions which benefit from blocking calcium ion channels. For instance, 3-aminopyrrolidine derivative III (IC50 at 0.067 Hz: 67 nM) was prepared via amidation of 6,6-bis-(4-fluorophenyl)hexanoic acid by (R)-(1-benzylpyrrolidin-3-yl)(methyl)amine, N-debenzylation, and subsequent amidation of the obtained aminopyrrolidine derivative by 3,5-di-tert-butyl-4-methoxybenzoic acid.

IT 861104-43-0P 861104-44-1P 861104-45-2P
861104-49-6P 861104-53-2P 861104-54-3P
861104-73-6P 861104-74-7P 861104-75-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-aminopyrrolidine derivs. useful as N-type calcium channel blockers)

RN 861104-43-0 CAPLUS

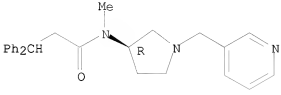
CN Benzenepropanamide, N-methyl-β-phenyl-N-[(3R)-1-(4-pyridinylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



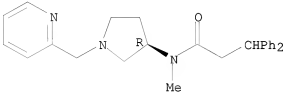
RN 861104-44-1 CAPLUS
CN Benzenepropanamide, N-methyl-β-phenyl-N-[(3R)-1-(3-pyridinylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



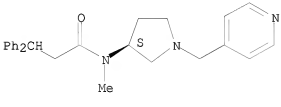

RN 861104-45-2 CAPLUS
CN Benzenepropanamide, N-methyl-β-phenyl-N-[(3R)-1-(2-pyridinylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



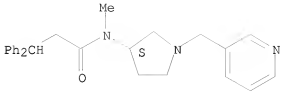

RN 861104-49-6 CAPLUS
CN Benzenepropanamide, N-methyl-β-phenyl-N-[(3S)-1-(4-pyridinylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



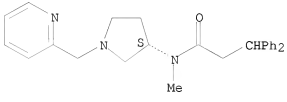

RN 861104-53-2 CAPLUS
CN Benzenepropanamide, N-methyl-β-phenyl-N-[(3S)-1-(3-pyridinylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



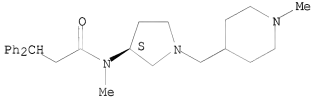
RN 861104-54-3 CAPLUS
CN Benzenepropanamide, N-methyl-β-phenyl-N-[(3S)-1-(2-pyridinylmethyl)-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



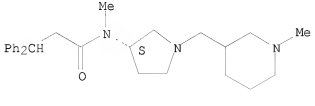
RN 861104-73-6 CAPLUS
CN Benzenepropanamide, N-methyl-N-[(3S)-1-[(1-methyl-4-piperidinyl)methyl]-3-pyrrolidinyl]-β-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 861104-74-7 CAPLUS
CN Benzenepropanamide, N-methyl-N-[(3S)-1-[(1-methyl-3-piperidinyl)methyl]-3-pyrrolidinyl]-β-phenyl- (CA INDEX NAME)

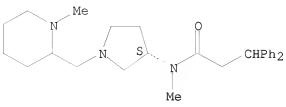
Absolute stereochemistry.



RN 861104-75-8 CAPLUS
CN Benzenepropanamide, N-methyl-N-[(3S)-1-[(1-methyl-2-piperidinyl)methyl]-3-

pyrrolidinyl]-β-phenyl- (CA INDEX NAME)

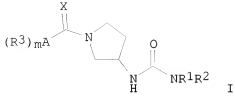
Absolute stereochemistry.




L9 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:347008 CAPLUS
DOCUMENT NUMBER: 142:411241
TITLE: Preparation of pyridinylcarbonylpyrrolidinylureas and related compounds as angiogenesis inhibitors.
INVENTOR(S): Haviv, Fortuna; Bradley, Michael F.; Sauer, Daryl R.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005035524 | A1 | 20050421 | WO 2004-US33169 | 20041008 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2540868 | A1 | 20050421 | CA 2004-2540868 | 20041008 |
| EP 1680415 | A1 | 20060719 | EP 2004-785388 | 20041008 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |

PRIORITY APPLN. INFO.: US 2003-682497 A 20031009
WO 2004-US33169 W 20041008
OTHER SOURCE(S): CASREACT 142:411241; MARPAT 142:411241
GI



I

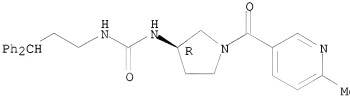
AB Title compds. [I; A = pyridazinyl, pyridinyl, pyrimidinyl, indol-3-yl, pyrazol-4-yl, pyrazinyl, isoxazol-4-yl, triazinyl; R1, R2 = H, alkenyl, alkoxy, alkoxyalkyl, alkyl, alkynyl, aryl, aralkyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, haloalkyl, heterocyclyl, heterocyclylalkyl, hydroxyalkyl, aminoalkyl, aminocarbonyl; R1R2N = atoms to form a (substituted) 5-7 membered ring; R3 = alkenyl, alkoxy, alkoxyalkyl, alkyl, alkoxycarbonyl, alkylcarbonyl, alkylsulfanyl, aryl, aralkyl, aryloxy, cyano, cyanoalkyl, cycloalkyl, heterocyclyl, OH, hydroxyalkyl, NO2, etc.; X = O, S; m = 0-4], were prepared Thus, (3R)-1-[(6-methylpyridin-3-yl)carbonyl]pyrrolidin-3-amine bistrifluoroacetate and Et3N in CH2Cl2 were treated with carbonyldiimidazole and after 5 h with benzylamine followed by stirring for an addnl. 4 h to give N-benzyl-N'-[(3R)-1-[(6-methylpyridin-3-yl)carbonyl]pyrrolidin-3-yl]urea. I inhibited human microvascular endothelial migration (HMVEC) by 48-99% at 0.1 nM.

IT 850212-49-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of pyridinylcarbonylpyrrolidinylureas and related compds. as angiogenesis inhibitors)

RN 850212-49-6 CAPLUS

CN Urea, N-(3,3-diphenylpropyl)-N'-[(3R)-1-[(6-methyl-3-pyridinyl)carbonyl]-3-pyrrolidinyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

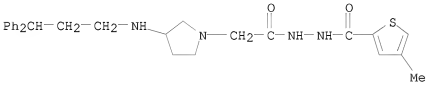
L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:791985 CAPLUS
DOCUMENT NUMBER: 141:342891
TITLE: Small molecule antagonists of the CCR2b receptor. Part 2: Discovery process and initial structure-activity relationships of diamine derivatives
AUTHOR(S): Moree, Wilna J.; Kataoka, Ken-ichiro; Ramirez-Weinhouse, Michele M.; Shiota, Tatsuki; Imai,

Minoru; Sudo, Masaki; Tsutsumi, Takaharu; Endo, Noriaki; Muroga, Yumiko; Hada, Takahiko; Tanaka, Hiroko; Morita, Takuya; Greene, Jonathan; Barnum, Doug; Saunders, John; Kato, Yoshinori; Myers, Peter L.; Tarby, Christine M.
CORPORATE SOURCE: Deltagen Research Laboratories, San Diego, CA, 92121, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(21), 5413-5416
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:342891

AB Structure-activity relationships (SAR) of a weakly active class of CCR2b inhibitors were utilized to initiate a lead evolution program employing the Drug Discovery Engine. Several alternative structural series have been discovered that display nanomolar activity in the CCR2b binding and CCR2b-mediated chemotaxis assays.

IT 774597-45-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(small mol. antagonists of CCR2b receptor: discovery process, preparation, and SAR of diamine derivs.)

RN 774597-45-4 CAPLUS
CN 1-Pyrrolidineacetic acid, 3-[(3,3-diphenylpropyl)amino]-, 2-[(4-methyl-2-thienyl)carbonyl]hydrazide (CA INDEX NAME)




REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

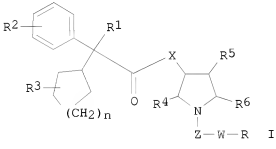
L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:546475 CAPLUS
DOCUMENT NUMBER: 141:106362
TITLE: Preparation of 1-substituted-3-pyrrolidine derivatives as muscarinic receptor antagonists
INVENTOR(S): Mehta, Anita; Gupta, Jang Bahadur; Sarma, Pakala Kumara Savithru
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | |
|---|---|---|---|
| WO 2004056767 | A1 | 20040708 | WO 2002-IB5590 | 20021223 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002347552 | A1 | 20040714 | AU 2002-347552 | 20021223 |
| EP 1583741 | A1 | 20051012 | EP 2002-783480 | 20021223 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| IN 2005DN03262 | A | 20071130 | IN 2005-DN3262 | 20050722 |
| US 20060194862 | A1 | 20060831 | US 2006-540245 | 20060207 |
| PRIORITY APPLN. INFO.: | | | WO 2002-IB5590 A | 20021223 |

OTHER SOURCE(S): CASREACT 141:106362; MARPAT 141:106362

GI




I

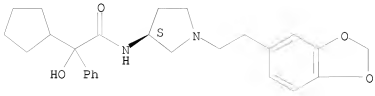
AB Title muscarinic receptor antagonists I (X = O, NH, etc.; R1 = OH, etc.; R2 = H, halo, alkyl; R3 = H, OH, etc.; R4, R5, R6 = H, alkyl; ; Z = CH2, SO2, carbonyl; W = alkylene, etc.; R = alkyl, aryl, etc.), useful for the treatment of various diseases of the respiratory, urinary and gastrointestinal systems mediated through muscarinic receptors, are prepared The affinity of these compds. for M2 and M3 muscarinic receptor subtype was tested. For example, (3S)-1-benzylpyrrolidin-3-yl cyclopentyl(hydroxy)phenylacetate was prepared and had pKi = 6.13/7.17 for the M2 and M3 receptor subtype resp.

IT 719278-60-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-substituted-3-pyrrolidine derivs. as muscarinic receptor antagonists)

RN 719278-60-1 CAPLUS

CN Benzeneacetamide, N-[(3S)-1-[2-(1,3-benzodioxol-5-yl)ethyl]-3-pyrrolidinyl]-α-cyclopentyl-α-hydroxy- (CA INDEX NAME)

Absolute stereochemistry.

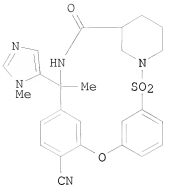



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:184902 CAPLUS
DOCUMENT NUMBER: 136:263181
TITLE: Macrocyclic inhibitors of prenyl-protein transferase
INVENTOR(S): Desolms, S. Jane; Shaw, Anthony W.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002020015 | A1 | 20020314 | WO 2001-US27013 | 20010830 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001090588 | A5 | 20020322 | AU 2001-90588 | 20010830 |
| PRIORITY APPLN. INFO.: | | | US 2000-230105P | P 20000905 |
| | | | WO 2001-US27013 | W 20010830 |

OTHER SOURCE(S): MARPAT 136:263181
GI



I

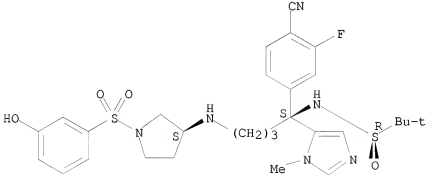
AB Piperidine- and pyrrolidine-containing macrocyclic compds. which inhibit prenyl-protein transferase and the prenylation of the oncogene protein Ras were prepared Thus, the macrocycles (14R,17R)- and (14R,17S)-I were prepared in multiple steps via fragment condensation. The products inhibited Ras farnesyl transferase with an IC50 of <1 μM.

IT 403825-47-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of macrocyclic inhibitors of prenyl-protein transferase)

RN 403825-47-8 CAPLUS

CN 2-Propanesulfinamide, N-[(1S)-1-(4-cyano-3-fluorophenyl)-4-[[(3S)-1-[(3-hydroxyphenyl)sulfonyl]-3-pyrrolidinyl]amino]-1-(1-methyl-1H-imidazol-5-yl)butyl]-2-methyl-, [S(R)]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:314672 CAPLUS
DOCUMENT NUMBER: 132:334358
TITLE: Preparation of pyrrolidine compounds as antagonists of serotonin 2 receptor
INVENTOR(S): Kuroita, Takanobu; Fujio, Masakazu; Nakagawa, Haruto

PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000026186 | A1 | 20000511 | WO 1999-JP6002 | 19991028 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2348879 | A1 | 20000511 | CA 1999-2348879 | 19991028 |
| AU 9963673 | A | 20000522 | AU 1999-63673 | 19991028 |
| EP 1125922 | A1 | 20010822 | EP 1999-951139 | 19991028 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| US 6468998 | B1 | 20021022 | US 2001-830718 | 20010501 |
| PRIORITY APPLN. INFO.: | | | JP 1998-311868 A | 19981102 |
| | | | WO 1999-JP6002 W | 19991028 |

OTHER SOURCE(S): MARPAT 132:334358
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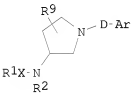


I

AB Described are pyrrolidine compds. represented by general formula [I; R1 = Q-Q5, etc. a proviso is given; R9 = H, C1-6 alkyl, C1-6 alkoxy, C1-6 hydroxyalkyl; X = CO, CS, NHCO, SO, SO2; R2 = H, alkyl, acyl, (un)substituted arylalkyl, (un)substituted aromatic ring, heterocyclic ring containing at least one atom selected from O, N, and S; D = C1-6 (un)substituted alkyl, alkenyl, etc], optically active isomers thereof or pharmaceutically acceptable salts of the same; and medicinal compns. containing the compds. of general formula I, optically active isomers thereof or pharmaceutically acceptable salts of the same together with pharmaceutically acceptable additives. These compds. have an antagonism to serotonin 2 receptor, a platelet aggregation inhibitory effect, a peripheral circulation improving effect and a lacrimal secretion promoting effect, which makes them useful as drugs for thromboembolism, dry eye, etc. Thus, 2-(4-fluorophenyl)ethyl p-toluenesulfonate and

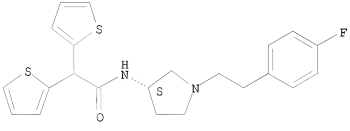
(S)-N-(pyrrolidin-3-yl)-1-adamantanecarboxamide were dissolved in DMF and stirred with K2CO3 at 70° for 5 h to give (S)-N-[1-[2-(4-fluorophenyl)ethyl]pyrrolidin-3-yl]-1-adamantanecarboxamide (II) which was converted into the HCl salt. II.HCl in vitro inhibited the binding of 3H-ketanserin to 5-HT2 receptor preparation from rat cerebral cortex synapse with IC50 of 0.18 nM vs. sarpogrelate. It in vitro showed IC50 of 1.9 μg/mL for inhibiting the collagen-induced rabbit blood platelet aggregation vs. 260 and 1,378 for sarpogrelate and cilostazol, resp.

IT 267644-10-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidine compds. as antagonists of serotonin 2 receptor for drugs)

RN 267644-10-0 CAPLUS

CN 2-Thiopheneacetamide, N-[(3S)-1-[2-(4-fluorophenyl)ethyl]-3-pyrrolidinyl]-α-2-thienyl- (CA INDEX NAME)

Absolute stereochemistry.




REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 44.08 | 532.29 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -6.40 | -25.60 |

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:07:23 ON 19 MAY 2008